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A SURVEY OF SOME VOLUNTARY BLOOD DONORS IN NEW SOUTH WALES.

By R. J. WALSH AND KATHLEEN CLEMENS.

From the New South Wales Red Cross Blood Transfusion Service, Sydney.

BLOOD TRANSFUSIONS are unique amongst all forms of therapy because they are entirely dependent on the services of human blood donors. No synthetic substitute for blood has yet been produced, or is likely to be produced. In Australia, as in some other countries, the increasing demands have been supplied entirely by voluntary effort. During the year 1955, 55,295 donations were made by the people of Sydney, who now number about 1,750,000.

No form of coercion or bribe has ever been offered in appeals for donors in New South Wales; no reward is given to the individual contributor, and the only recognition is the presentation of a certificate and a badge, which are valued by some and ignored by others. Details of the use of individual contributions are not supplied to the donors, who remain anonymous to the recipients. When a donor has once given his blood he is asked to continue, and after an interval of three months is notified that he is eligible to contribute again.

There is probably no form of voluntary social service today which affects so many people as the giving of blood; nor is there anything more altruistic in its objects. It is true that many blood donors derive considerable satisfaction from the fact that they have undertaken something which many of their fellow-men have not; often, therefore, they derive some elation from their sense of achievement. On the other hand, their efforts are not without some cost in terms of inconvenience, physical discomfort, transport and domestic activities.

It is perhaps surprising that there has not been a comprehensive investigation of the social and psychological aspects of blood donors, and in particular of the factors which move them to give their blood. The writers make no claim for the completeness of the investigation, which has been conducted in the New South Wales Red Cross Blood Transfusion Service; but some of the facts presented in this report are of interest.

The Investigation.

The investigation was conducted in three parts, as follows: A: new volunteers were questioned; B: the records of blood donors who had enrolled several years previously were examined; C: the record of every blood donor who attended the centre during two months in 1954 was examined.

Part A.

Two hundred and forty-five volunteers who had not previously given blood were asked what factor or factors had

been mainly responsible for their becoming blood donors. The results of this survey are shown in Table I.

These findings were somewhat unexpected. The relatively low percentage who were friends or relatives of recipients of blood or serum was surprising, but has been confirmed on several other occasions. Radio and newspaper appeals at the time of this survey were not urgent in their nature. They were incorporated as news items and not as advertisements, which are considered to be of little value. Advertisements for blood donors seem to be even less effective than appeals by means of posters in trams, trains, ferries or shop windows. Those who stated that they had witnessed the use of transfusions were either members of hospital staffs, or patients in hospital, though not themselves recipients of blood. This reason for volunteering to become blood donors had not been anticipated. It can be seen, however, that the majority were friends or relatives of blood donors. Some may have become donors themselves merely from a desire to emulate these friends; others probably because it has been explained to them that the process of giving blood is simple and not painful.

TABLE I.

Reasons Given by Volunteers for Enrolling as Blood Donors.

Reason.	Number.	Percentage.
Through contact with other donors ..	109	44·5
Friends or relatives of patients who have received blood	20	8·2
Radio appeals	40	16·3
Newspaper appeals	50	20·4
Poster appeals	10	4·1
Through contact with transfusion work	16	6·1
Total	245	99·6

Part B.

The records of 351 male and 565 consecutive female volunteers who became donors in 1941 were examined. They were analysed according to age and the total number of donations that they had given. The results are shown in Table II. It will be seen that in both sexes most age groups are evenly represented, but that 61·7% of the total were females.

The records of 942 consecutive donors who enrolled in 1948 were similarly examined, with the results shown in Table III. At this time there was a reversal of the sex distribution, 552 donors or 58·6% being males. It is to be noted that in both sexes the age distribution has changed since 1941.

Figure I has been drawn from the data in Tables II and III, and is designed to show the wastage rate amongst donors. It also includes data for donors who enrolled in 1951. The abscissa represents the number of donations and the ordinate the percentage of volunteers who have given blood once, twice or more times during the subsequent years. Thus of the series of 351 males who first donated blood in 1941, 82% returned on a second occasion, approximately 45% acted as donors five times, and approximately 21% gave 10 or more donations. Essentially similar results were obtained in the three groups, and in none was there a significant difference between the sexes. It should be mentioned that there was no special appeal for blood donors during the periods in which any of the three groups of donors were enrolled.

The wastage rate as shown in the tables and the graph is of great interest. The shape of the curve is probably characteristic of most forms of voluntary human activity, whether social or charitable in nature. Initial enthusiasm is later modified by circumstances, or by rival interests. Man is a gregarious animal, and a desire for a multiplicity of interests and experiences is strongly developed, especially in younger people. The variations between the activities of different people are well shown by these figures. A few amongst us maintain interest and display continued activity in one or a very few fields—the blood donors who give their blood on numerous occasions; a few rapidly lose interest and discontinue a particular activity—the donors who serve only on one occasion; and the majority lie in positions between the two extremes, offering a moderate amount of assistance, perhaps to several activities.

From a practical point of view it would assist greatly if the curves in Figure I could be altered so that the slope was less pronounced. There is no doubt that measures directed to this end are possible, and an attempt was made to ascertain the best approach by investigating some of the defaulters. A *questionnaire* was sent to 3649 donors who had not responded to four or more calls. Replies were received from 644 (17·6%), but 59 were returned by the postal authorities because they could not be delivered. Some "wastage" amongst the donors was therefore due to the failure to leave a forwarding address when changing residence or place of employment.

Of the 644 who returned the *questionnaire*, 329 stated that they would continue as donors. The remaining 315 stated that they were no longer available, and an analysis of the reasons given was as follows: ill health, 39·9%; pregnancy, 4·9%; no longer accessible, 27·6%; hours of work, 3·1%; no reason given, 9·1%; deceased, 2·1%; ill effects following blood donations, 2·8%; temporarily unavailable, 2·4%; miscellaneous reasons, 8·0%.

The high percentage offering ill health as the reason for discontinuing is of interest. Anæmia was one of the most commonly stated complaints; but a low hæmoglobin value on the occasion of the last visit was recorded in relation to only one of 14 such donors whose records were examined. There is a regrettable tendency on the part of many medical practitioners to ascribe to anæmia any vague symptoms which may appear in blood donors. Without confirming the diagnosis with a hæmoglobin estimation or a red cell count, they advise patients not to continue as blood donors.

Another point of interest from the analysis is the high percentage who advised that inaccessibility was responsible for discontinuance. In New South Wales, as throughout Australia, the bulk of the blood is collected in the capital city. A mobile operating team visits outer suburbs and some country towns, but many areas to which blood donors may transfer are not included in the itinerary. It should be pointed out, lest the foregoing results be interpreted as indicating the desirability of extending the activities of the mobile team, that the number of donors who replied in this way represented only 2·3% of those to whom the *questionnaire* was sent.

To obtain some indication of the economic and social status of the volunteers, an analysis was made of occupations as stated on the enrolment forms. The Acting Commonwealth Statistician of Australia kindly supplied figures for the occupational groupings of both males and females in the Sydney metropolitan area as ascertained in the 1947 Census. Occupations were grouped in 10 orders (Table IV).

The figures in Table IV concern only those between the ages of eighteen and sixty years. They compare the distribution of both male and female donors in the years 1949, 1951 and 1953. It will be seen that amongst the male donors (*a*) the professional and semi-professional order is better represented than in the general population; (*b*) the administrative (executive and managerial) order is not well represented; (*c*) there has been a progressive increase amongst donors who belong to the commercial and clerical sections of the community; and (*d*) there has been a progressive decrease in the representation of the operatives and skilled artisans. The last two observations are probably explained by the fact that commercial and clerical workers are for the most part employed in the inner part of the city and usually are individually not essential for continuous work, whereas artisans are predominantly employed in the outer parts of the city, and this entails considerable and often excessive travel to the static blood-collecting centre, with consequent loss of time from processes dependent on teams. It seems likely that this trend

TABLE II.

Donors who Enrolled in 1941.

Age Group. (Years.)	Number of Donations before Discontinuing. 1	2	3	4	5	6	7	8	9	10 and Over.	Total.	Percentage.
Males.												
Up to 19 ..	14	4	5	5	1	1	2	—	1	1	34	9·7
20 to 29 ..	16	14	9	3	4	3	6	4	2	15	76	21·6
30 to 39 ..	13	16	10	13	3	6	7	—	2	16	86	24·5
40 to 49 ..	8	12	13	5	7	6	—	6	3	19	79	22·5
50 to 59 ..	8	6	4	9	6	4	4	4	3	21	69	19·6
60 and over	1	3	1	—	—	—	1	—	—	1	7	2·0
Total ..	60 (17·1%)	55 (15·7%)	42 (12·0%)	35 (10·0%)	21 (6·0%)	20 (5·7%)	20 (5·7%)	14 (4·0%)	11 (3·1%)	73 (20·8%)	351	100·0
Females.												
Up to 19 ..	20	16	5	6	5	3	1	1	6	6	69	12·2
20 to 29 ..	31	34	29	19	6	3	8	4	3	18	155	27·4
30 to 39 ..	22	20	6	12	8	5	9	4	3	23	112	19·8
40 to 49 ..	24	15	9	10	13	5	5	4	2	28	115	20·4
50 to 59 ..	18	17	18	10	10	5	4	3	4	17	106	18·8
60 and over	4	2	—	—	—	—	—	—	1	1	8	1·4
Total ..	119 (21·1%)	104 (18·4%)	67 (11·9%)	57 (10·1%)	42 (7·4%)	21 (3·7%)	27 (4·8%)	16 (2·8%)	19 (3·4%)	93 (16·5%)	565	100·0

TABLE III.

Donors who Enrolled in 1948.

Age Group. (Years.)	Number of Donations before Discontinuing. 1	2	3	4	5	6	7	8	9	10 and Over.	Total.	Percentage.
Males.												
Up to 19 ..	7	10	5	3	3	5	4	2	1	20	60	10·9
20 to 29 ..	64	45	27	23	15	16	14	6	13	31	254	46·0
30 to 39 ..	22	22	11	9	9	7	7	3	5	20	124	22·4
40 to 49 ..	12	10	9	9	3	3	2	3	1	24	76	13·8
50 to 59 ..	7	3	8	4	3	1	1	3	1	7	38	6·9
60 and over	—	—	—	—	—	—	—	—	—	—	—	—
Total ..	112 (20·3%)	90 (16·3%)	60 (10·9%)	48 (8·7%)	33 (6·0%)	32 (5·8%)	28 (5·1%)	17 (3·1%)	21 (3·8%)	111 (20·1%)	552	100·0
Females.												
Up to 19 ..	14	14	15	3	3	5	5	4	2	12	77	19·7
20 to 29 ..	34	30	20	13	17	13	4	2	3	12	148	38·0
30 to 39 ..	20	11	11	5	6	2	1	4	3	15	78	20·0
40 to 49 ..	9	10	5	5	6	5	3	2	1	10	56	14·3
50 to 59 ..	9	2	5	1	1	—	1	1	3	7	30	7·7
60 and over	1	—	—	—	—	—	—	—	—	—	1	0·3
Total ..	87 (22·3%)	67 (17·2%)	56 (14·3%)	27 (6·9%)	33 (8·5%)	25 (6·4%)	14 (3·6%)	13 (3·3%)	12 (3·1%)	56 (14·4%)	390	100·0

will continue, and that recruiting of new blood donors will most profitably be undertaken amongst city workers.

Among females also the commercial and clerical occupations contributed a high percentage of the donors in all three years, and a striking observation from Table IV is the relatively small and perhaps decreasing percentage of female donors from "persons not in the work force", which includes the housewives. In this last regard it is probable that the 1947 Census figures are not representative of the occupation distribution in subsequent years. There is a general impression that in later years an increasing number of housewives have undertaken part-time or full-time gainful employment; unfortunately the 1954 Census figures have not been dissected for the Sydney metropolitan area to confirm this probable trend. However, the difficulty and expense of travel and the care of children almost certainly prevented many housewives from attending the blood-collecting centre.

The occupational groupings of donors have also been dissected for both sexes according to age groups, and have been compared with the corresponding figures from the 1947 Census. The general pattern of Table IV is seen in all the different age groups.

Part C.

Part B above represents an analysis of volunteers who enrolled as donors in different years, and is an attempt to ascertain factual information concerning occupational

TABLE IV.

Percentages in Each Occupational Order of the Population in the Sydney Metropolitan Area and of Blood Donors.

Order.	Census (1947).		Donors (1949).		Donors (1951).		Donors (1953).	
	Male.	Female.	Male.	Female.	Male.	Female.	Male.	Female.
Rural, fishing and hunting occupations ..	1·0	0·04	1·1	0·0	0·7	0·0	0·05	0·0
Professional and semi-professional	3·9	3·2	4·5	9·5	5·0	11·8	5·1	9·0
Administrative	6·5	1·6	3·3	0·3	4·1	0·2	2·7	0·9
Commercial and clerical	19·2	12·1	22·2	31·6	28·3	25·3	34·7	44·6
Domestic and protective occupations ..	6·5	3·9	9·7	5·7	6·5	6·7	7·6	4·4
Craftsmen	23·7	0·8	25·4	0·7	26·0	0·7	28·3	0·7
Operatives	24·2	7·6	20·7	8·6	15·5	8·6	11·8	6·4
Labourers	5·5	0·02	6·0	0·0	5·0	0·0	5·2	0·0
Occupation indefinite and not stated ..	2·8	1·2	1·3	1·2	1·6	1·5	1·8	2·4
Persons not in the work force	6·7	69·6	5·9	42·5	7·4	45·2	2·2	31·6

groupings, sex and age distribution and the subsequent records as donors. In Part C groups of currently active donors have been analysed in the same way to show whether the information in Part B is representative of the picture several years later.

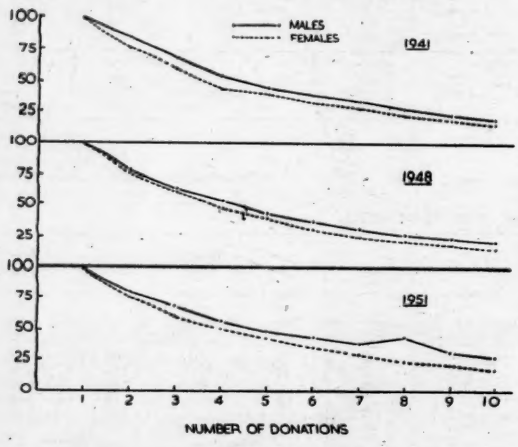

FIGURE I.

The "wastage" rate amongst blood donors who volunteered in three different years. The percentage of the original volunteers who gave a varying number of donations is shown.

The records of 1831 male and 754 female donors who gave blood at the main blood-collecting centre during June and July, 1954, were analysed according to age and the total number of donations given. The age distribution is shown in Table V and the number of donations in Figure II.

These analyses clearly show the following facts:

1. The trend in sex distribution at time of enrolment—females predominating in 1941, males predominating in later years—continued during 1954. Of donors actually attending in 1954, 70·8% were males. It should be mentioned that during the time covered by this analysis there was no special appeal or other publicity activity.

2. There are many more male donors aged under forty years than over that age, the maximum number being in the twenty-five to twenty-nine years group. Amongst females the distribution is more even. The maximum number is in the twenty to twenty-four years group, but there are approximately equal numbers in the other groups except the fifty-five to fifty-nine years group. The sustained interest of the females in the older age groups was an unexpected finding in view of the age distribution at the time of enrolment (Tables II and III).

3. The wastage rate is evident from Figure II. Generally there is a progressive decrease in the number of donors who have given increasing numbers of donations. This emphasizes the need for continued replacement of donors. The minor fluctuations that are seen in Figure II are almost certainly due to the fact that the rate of enrolment is not constant, being stimulated at times by special appeals.

TABLE V.

Age Distribution of Blood Donors Attending in June-July, 1954.

Age Group. (Years.)	Males.		Females.	
	Number.	Percentage of Total.	Number.	Percentage of Total.
18 to 19	62	3·4	42	5·6
20 to 24	265	14·5	136	18·0
25 to 29	358	19·6	81	10·8
30 to 34	345	18·8	76	10·2
35 to 39	245	13·4	90	11·9
40 to 44	212	11·6	95	12·5
45 to 49	146	8·0	97	12·9
50 to 54	123	6·7	80	10·6
55 to 59	65	3·5	50	6·6
60 to 64	10	0·5	7	0·9
Total	1831	100·0	754	100·0

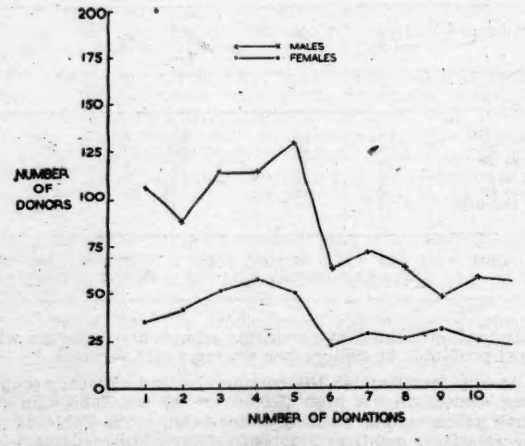

FIGURE II.

An analysis of the number of donations given by 1831 male and 754 female donors in an unselected series during 1954.

4. A dissection of the number of donations discloses that there are no significant differences between the age groups with the exception of the younger volunteers, who have not yet had time to prove their endurance.

Discussion.

The information presented in this report represents a collection of statistical facts concerning blood donors. An attempt has been made to explain some of the more important findings, particularly in relation to the practical problem of recruiting blood donors. However, no investigations have yet been made into two fundamental but related problems which may have practical importance. These are, firstly, the factors motivating a person to become a blood donor and then to continue his services, and secondly, the factors which inhibit many people from offering their blood.

An investigation of these matters would be a difficult task, and would be performed most appropriately by a psychologist. At present general impressions only are available; but it seems reasonably certain that fear in some form or other inhibits many otherwise willing volunteers. Some fear the consequences of blood removal and particularly the embarrassment of possible syncopal attacks, others the supposedly associated discomfort, and still others the medical atmosphere of a blood-collecting centre. A thorough investigation of the problems would be difficult, because many people would plead insufficient time, pressure of work and the like as an excuse for their failure to give blood. These are probably forms of rationalization for fear, lethargy or selfishness, and would have to be carefully analysed by a trained investigator. Although the problems are difficult, they are not insoluble, and much practical and fundamental information would be obtained.

Summary.

Statistical information concerning the age and sex distribution and occupations of blood donors in New South Wales has been collected. Attempts have also been made to investigate the factors encouraging the enrolment of donors, the reasons why some discontinue at various intervals after first giving blood, and the rate of "wastage" in different years.

A large number volunteer because of close association with others who have been donors; but there are proportionately few relatives and friends of recipients of blood. The "wastage" rate has been constant over the years. Lack of interest is probably the most important reason why donors discontinue; but ill health, pregnancy, transfer from the city and other such factors have been responsible for losses. Although all occupational groups are well represented, there has been in recent years amongst male donors an increased representation from the "commercial and clerical" group and a decreased representation from the "operatives" group. There has also been a decreased representation from the housewives and a proportionate increase from the female "commercial and clerical" group. A number of socio-economic factors are probably responsible for these trends and for a reversal of the sex ratio amongst the donors, males providing approximately 70% of the requirements in later years.

FŒTO-MATERNAL TRANSFUSION: ANOTHER CAUSE OF POST-HÆMORRHAGIC ANÆMIA IN THE NEWBORN.[1]

By JOHN H. COLEBATCH, DAVID PITT AND T. G. MADDISON,

From the Royal Women's Hospital and the Royal Children's Hospital, Melbourne.

A GENERATION ago anæmia in a newborn baby was usually sufficient cause for a very grave prognosis; the Rh factor had not then been discovered, and even a simple blood transfusion was a technically hazardous undertaking. In the last ten years, with the introduction of the Coombs test and exchange transfusions, neonatal anæmia has lost much of its former peril. So streamlined and so successful is the modern treatment of erythroblastosis becoming that there is now a real danger of falling into the trap of oversimplifying the problem of neonatal anæmia.

It is necessary first to have a clear picture of what constitutes anæmia in the earliest weeks of life, and this picture must be based on a knowledge of the range of the hæmoglobin level and of the red cell count in normal infants. Experience at the Royal Women's Hospital suggests that the hæmoglobin levels of normal infants in Melbourne are in line with the figures of overseas workers quoted by Walsh *et alii* (1953) (Figure I). This means

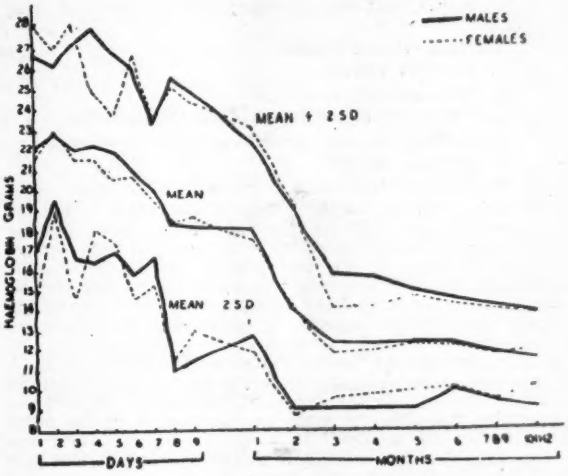

FIGURE I.

The mean *plus* and *minus* twice the standard deviation of the hæmoglobin values of infants. The age of the infants plotted on the abscissa is not constant. (From Walsh *et alii*, 1953; reproduced by permission.)

that in the critical first two days of life a hæmoglobin level of less than 17 grammes per 100 millilitres (117%) probably, and less than 16 grammes per 100 millilitres (110%) definitely, indicates anæmia. These are the figures for peripheral blood, taken from finger or heel prick; cord blood levels are usually at least two grammes or 14% lower.

When an infant in the first two days of life has anæmia it is natural to think first of *erythroblastosis fœtalis*, because this is certainly the commonest cause. In this condition the diagnosis is usually easy to establish from the clinical features, the blood picture, the Coombs test result and the maternal antibody titre levels. A negative result from the Coombs test carefully performed on cord blood excludes erythroblastosis due to Rh incompatibility (which accounts for 90% to 95% of examples of this disease). In the proportion of cases due to ABO incompatibility there is usually a negative result to the Coombs test, and their diagnosis requires detailed serological study. Very occasionally this disease is caused by maternal sensitization to less well-known blood group antigens, such as the Kell and the Duffy factors; this was so recently in one infant in the neonatal ward of the Royal Children's Hospital, Melbourne, whose blood contained an antigen not previously identified.

In at least 5% of cases, however, anæmia in the first two days after birth is not due to *erythroblastosis fœtalis*. Unless this is recognized the infant is likely to suffer from incorrect treatment and may consequently die. For prac-

[1] Read at a meeting of the Pædiatric Society of Victoria on December 14, 1955.

tical purposes the non-hæmolytic anæmias at this age are limited to those caused by hæmorrhage; only in very rare instances are such conditions as syphilitic and other infections, neoplasms and leuchæmia responsible.

Mechanisms of Neonatal Hæmorrhage.

Post-hæmorrhagic anæmia in this early neonatal period has been referred to by obstetricians for many years, though doubtless some cases formerly labelled thus were really examples of unsuspected *erythroblastosis fœtalis*. In addition to hæmorrhagic disease of the newborn, trauma and intracranial hæmorrhage, it is now recognized that there are at least six mechanisms by which hæmorrhage may arise from the region of the placenta. These may be set out as follows:

Post-Hæmorrhagic Anæmia in the Early Neonatal Period: Mechanisms of Production.

1. Intracranial hæmorrhage; trauma; slipped cord ligature.
2. Hæmorrhagic disease.
3. *Placenta prævia.*
4. *"Placenta previa cesarea".*
5. Premature separation or *abruptio placentæ.*
6. *Vasa prævia* with or without velamentous insertion.
7. Rupture of cord.
8. Ruptured vessels in fœtal part of placenta.

Placenta prævia occurs in 1% of all pregnancies, and its diagnosis is not difficult for the obstetrician. At the Royal Women's Hospital stillbirth or neonatal death occurs in 17% of cases of *placenta prævia*, and in the mother sufficient bleeding occurs to necessitate blood transfusion for her in at least half the cases; yet the newborn infant rarely has much anæmia if delivered *per vaginam*. *"Placenta previa cesarea"* is the term coined by De Lee for the placenta so placed that the obstetrician finds it difficult to avoid damaging it in the operation of Cæsarean section. Damage to the placenta, whether by incision or otherwise, may lead to rapid exsanguination of the fœtus even if delivery is rapid. In a recent case the infant had been thought to have *asphyxia pallida* because he was pale and limp after birth; but recovery was slow, and a few days later a hæmoglobin level of only 13 grammes per 100 millilitres (89%), falling to 11 grammes per 100 millilitres at two weeks, pointed to the diagnosis of post-hæmorrhagic anæmia. Useful descriptions of this condition, particularly of its obstetrical aspects, have been given recently by Neligan and Russell (1954), by Butler and Martin (1954) and by F. Novak (1953). *Abruptio placentæ* or premature separation of the placenta, wherever it is placed in the uterus, is also a possible cause of post-hæmorrhagic anæmia in the infant; but a much greater risk with this condition is from the fœtal anoxia which it causes. The diagnosis of the rare condition of *vasa prævia* requires a careful inspection of the placenta and cord. The condition is usually associated with a velamentous insertion of the cord or with other anatomical abnormalities such as bipartite or tripartite placenta, *placenta succenturiata* and battledore placenta. Rupture of the unprotected vessels can readily occur, causing severe hæmorrhage with at least a 50% risk of stillbirth or death within a few hours of birth. Rupture of the cord itself is another rare cause to be mentioned.

These mechanisms do not account for all cases of post-hæmorrhagic anæmia in the newborn, and it was a serologist, Alexander Wiener (1948), who suggested that severe anæmia might be caused by "unapparent hemorrhage from the fetal surface of the placenta" into the mother's circulation. He described three cases in which the infant was very pale at birth, with weak cord pulsations and a hæmoglobin value of less than nine grammes per 100 millilitres; two of the infants died, even though blood transfusion had been commenced within two to three hours of birth. Wickster (1952) followed this up with a comprehensive review of post-hæmorrhagic shock in the newborn, describing six new cases, one of which appeared to be an example of Wiener's (then hypothetical) occult bleeding from the fœtal into the maternal circulation. Carl Smith (1953) presented four cases of non-hæmolytic anæmia in the newborn for which he postulated marrow hypoplasia as the cause, on rather slender evidence. Laski and Johnston (1954), on the other hand, described 22 cases of non-hæmolytic anæmia in newborn infants admitted to Toronto Hospital for Sick Children over a seven-year period; the causes were not stated, but the bone marrow was normal in the five fatal cases.

The proof of Wiener's exciting hypothesis—that anæmia in the fœtus or newborn might be caused by the rupture of villi, sinuses or capillaries from the fœtal into the maternal part of the placenta with unsuspected and inapparent fœtal hæmorrhage—was finally provided eighteen months ago by Bruce Chown (1954*b*), Professor of Pædiatrics in Winnipeg. In an infant born after a normal pregnancy and labour, with a hæmoglobin value of 7·8 grammes per 100 millilitres and numerous erythroblasts in the blood, Chown reported a negative result from the direct Coombs test, but agglutination with an indirect Coombs test when blocking anti-D serum was used with the cells of the mother, whose blood did not contain the D antigen. He then applied differential agglutination techniques, tests for absorption of anti-D by the mother's blood, and biochemical estimation of the amount of fœtal or refractory hæmoglobin in the mother's blood. Thus he established beyond reasonable doubt that 5% to 10% of the red cells in that mother's circulation were derived from her unborn infant. At an American Pediatric Society meeting Chown (1954*a*) described this and two similar cases, in one of which a gross placental defect was thought to be the site of the fœto-maternal transfusion. In the ensuing discussion it was suggested that fœtal hæmoglobin

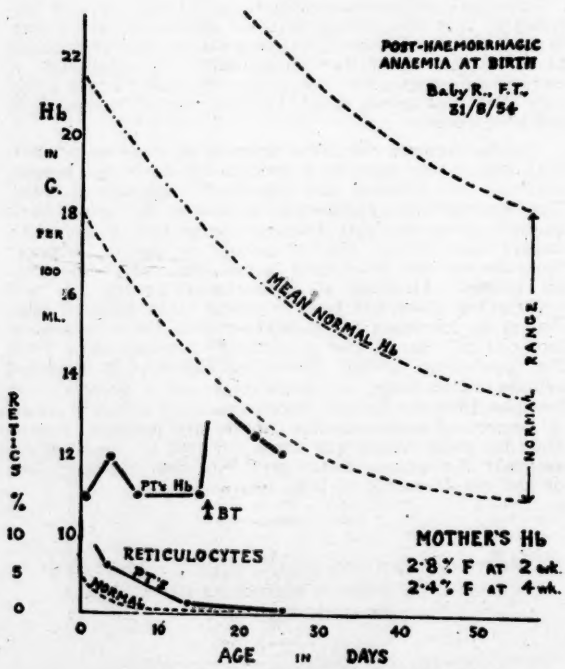

FIGURE II.

estimations, both on the mother's circulating blood and on the blood lost by her *per vaginam*, would prove most valuable in diagnosis. This idea has been tested in part in the following three cases.

Reports of Cases.

CASE I.—In August, 1954, an unmarried *primigravida* under the care of Dr. George Simpson was given a medical induction of labour; confinement was two weeks "overdue". After

a perfectly normal labour lasting eleven hours, she was delivered of a baby weighing nine pounds four ounces, who was cyanosed at first, but revived rapidly. Later he was noted to be very pale; twenty-eight hours after his birth, the hæmoglobin level was only 11·0 grammes per 100 millilitres (76%). There was no jaundice, the spleen was not palpable, the liver was of normal size, the result of the direct Coombs test was negative, no Rh antibodies were detected in the mother's serum, and no incompatibility between the infant's cells and the mother's serum was detected. The blood groups of mother and infant were identical (B, Rho+, Rh'+, Rh"−). On the third day a full blood examination revealed considerable anisocytosis with a colour index of 1·09, an increased reticulocyte level of 6%, and 16 late erythroblasts per 100 leucocytes; the platelets and leucocytes were normal. Normal results were obtained to Kline and Wassermann tests of the mother, and from radiographic examination of the infant's long bones.

With this evidence against such possible diagnoses as *erythroblastosis fœtalis* and syphilis, it was considered that the abnormal erythropoiesis pointed to a post-hæmorrhagic anæmia. Of the mechanisms listed in the tabulation given earlier, fœto-maternal transfusion seemed the probable one in this case. It was found that at two weeks after delivery 2·8% of the mother's hæmoglobin was of fœtal type, and at one month the proportion had fallen to 2·4%.[1] At this stage the mother's departure to another State made further observation impossible. The infant, whose only symptoms had been pallor and irritability, was given a small blood transfusion in the third week after the investigations had been carried out, and when last examined two weeks later he was quite well. The relevant hæmatological findings in this case are set out graphically in Figure II.

CASE II.—The mother in this case had six living children, but her obstetrical history was bad—one breech delivery at full term, then five premature deliveries, then two pregnancies ending in miscarriage at four to five months. In her ninth pregnancy, under the care of Dr. W. J. Rawlings, she was given a blood transfusion for nutritional anæmia at twenty-nine weeks, two external versions were performed, and a spontaneous normal, though premature, labour occurred at thirty-two weeks in February, 1955. The infant, a female, weighed three pounds nine and a quarter ounces at birth, and she responded normally to the routine care of the premature babies' nursery. Routine testing at the age of one month showed that her hæmoglobin level was only 9·5 grammes per 100 millilitres (66%), and by the seventh week it had fallen to 7·5 grammes per 100 millilitres (51%). The results of hæmatological investigations were otherwise normal, and the blood groups of both mother and infant were A, Rh+.

Six weeks after delivery it was found that 2·3% of the mother's hæmoglobin was of fœtal type. The results of subsequent estimations were as follows: 1·2% at eleven weeks, 1·2% at fifteen weeks, 0·5% at twenty-seven weeks. The infant was symptomless and seemed to be thriving on an iron-fortified dried milk feeding, so she was not given a blood transfusion. Later, however, feeding problems due to the mother's emotional instability produced a nutritional hypochromic anæmia so readily that in retrospect it was considered that it would have been wiser to give the infant a blood transfusion or at least more intensive iron therapy at the earlier stage in order to prevent iron depletion. The hæmatological findings in this case are set out in Figure III.

CASE III.—The mother, after two normal pregnancies, had hypertension and œdema in the later weeks of her third pregnancy. Labour was successfully induced by artificial rupture of the membranes at term; but delay in the second stage led to delivery by Cæsarean section in a rural hospital in September, 1955. The infant, a female, weighed six and a half pounds at birth, and a regular respiratory rhythm was established within five minutes. However, she was "very pale and floppy" throughout the first day, and vomited a feeding given at fifteen hours; her pulse rate was not recorded.

When admitted to the Royal Children's Hospital early on the second day, the infant was in such poor condition, with a hæmoglobin level of 8·9 grammes per 100 millilitres (60%) and a few scattered petechiæ, that a blood transfusion was given almost immediately. Thereafter the infant recovered rapidly and completely. Owing to the circumstances, full hæmatological investigation was unfortunately not carried out. However, there was no evidence of thrombocytopenia, and *erythroblastosis fœtalis* was not suggested by the history, by the clinical features or by the blood groups of mother and infant. Investigation of the mother's hæmoglobin showed that on the fourth day 2·4% of it was of fœtal type, while at one month after delivery none of her hæmoglobin was of this type.

[1] The alkali denaturation method of Singer has been used for the estimation of fœtal hæmoglobin in this study.

Discussion.

The clinical evidence alone may justify a provisional diagnosis of post-hæmorrhagic anæmia in the newborn, but it must be appreciated that the clinical features will vary with the severity of the hæmorrhage. In mild cases

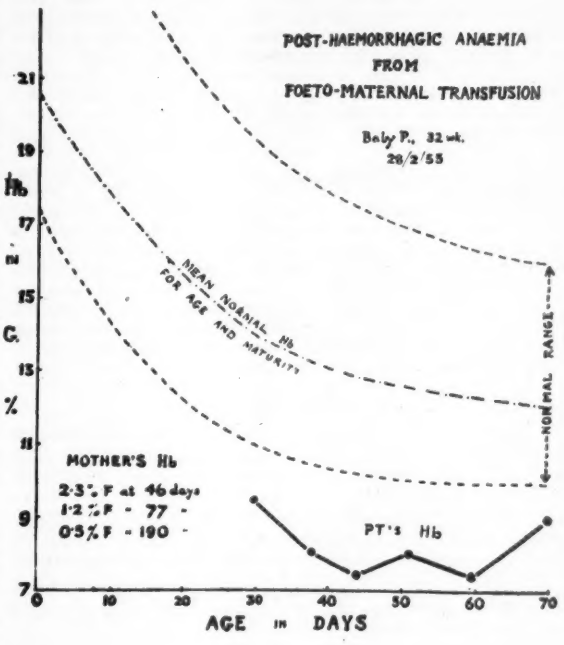

FIGURE III.

there may be no symptoms, and the condition may be detected only by a routine check, perhaps late in the neonatal period as in Case II. More severe hæmorrhage will necessitate a blood transfusion, usually at an earlier stage. Sometimes the hæmorrhage may be so severe that unless a blood transfusion is commenced very promptly, even within a matter of minutes after delivery, the infant will certainly die. It is likely also that the hæmorrhage can be sufficiently sudden and profuse to cause stillbirth, possibly with a reaction in the mother, as Chown has suggested in cases of fœto-maternal transfusion.

It is thus important to bear in mind the usual clinical features by which post-hæmorrhagic anæmia may be recognized in the first two or three days of life. These may be set out as follows:

Post-Hæmorrhagic Anæmia in Early Neonatal Period: Usual Clinical Features.

1. Pallor.
2. Weakness, loss of tone.
3. Tachycardia.
4. No unexpected jaundice.
5. No pathological enlargement of liver or spleen.
6. Oxygen of little benefit.
7. Transfusion has dramatic effect.

Erythroblastosis fœtalis can be diagnosed as a rule from the family history, the mother's blood group and titre of specific antibodies, the response to the direct Coombs test on cord blood, and the infant's blood group and clinical features. Prolonged cerebral anoxia (with *asphyxia pallida*) and cerebral trauma will also cause pallor and

loss of muscle tone; but in these disorders the pulse rate is usually normal or slow, cerebral signs are present, atelectasis almost invariably occurs, and oxygen administration improves the colour. The details of the labour and of the appearance of the cord and placenta can be expected to provide confirmation of the diagnosis of post-hæmorrhagic anæmia, except when the fœtus had bled into the mother's circulation.

The diagnosis of the newly discovered entity, fœto-maternal transfusion, can be established by finding in the mother's circulating blood an abnormally high proportion of fœtal hæmoglobin, which gradually disappears in subsequent weeks. The experience of Melbourne workers is in keeping with the statement of Singer (1951) that the proportion of fœtal hæmoglobin in the blood of normal adults varies from nil to 1·7%. At the Royal Children's Hospital, in the hæmatological laboratory of the Department of Pathology, Miss Betty Wilson has recently tested for us the blood of six normal women during the first week of the puerperium; the proportion of fœtal hæmoglobin present varied from 0·1% to 1·2%, with a mean of 0·8%. It is therefore justifiable to regard as abnormal the results of the first estimations of fœtal hæmoglobin in the three cases reported here, and this is substantiated in each case by the subsequent decrease in the amount of fœtal hæmoglobin. These three cases were encountered by one team in a period of thirteen months, which supports the view of no less an authority than Dr. Clement Smith that "this is something that we have all seen more often than we know".

Summary.

1. Attention is drawn to the important condition of post-hæmorrhagic anæmia in the early neonatal period, with particular regard to the mechanism of its production and to its diagnosis.

2. Fœto-maternal transfusion is discussed—a recently discovered variety of post-hæmorrhagic anæmia caused by hæmorrhage from the fœtal into the maternal circulation.

3. Three cases of fœto-maternal transfusion are presented, diagnosed by estimation of fœtal hæmoglobin in the mother's blood.

Acknowledgements.

This study would not have been possible without the help of Miss Betty Wilson, Mr. Ian Parsons and Dr. J. Santamaria in carrying out the estimations of fœtal hæmoglobin. We are also indebted to Dr. George Simpson and Dr. W. J. Rawlings for permission to publish their cases.

References.

BUTLER, N. R., and MARTIN, J. D. (1954), "Anæmia of Newborn following Anterior Placenta Prævia", *Brit. M. J.*, 2: 1455.

CHOWN, B. (1954*a*), "Three Unusual Cases of Anemia of the Newborn", *Am. J. Dis. Child.*, 88: 508.

CHOWN, B. (1954*b*), "Anæmia from Bleeding of the Fetus into the Mother's Circulation", *Lancet*, 1: 1213.

LASKI, B., and JOHNSTON, W. H. (1954), "22 Cases of Non-hemolytic Neonatal Anemia", *Am. J. Dis. Child.*, 88: 811.

NOVAK, F. (1953), "Posthemorrhagic Shock in Newborns during Labor and after Delivery", *Acta med. iugoslav.*, 7: 280; quoted in "Year Book of Pediatrics, 1955-56", Chicago, 23.

SINGER, K., CHERNOFF, A. I., and SINGER, L. (1951), "Studies on Abnormal Hemoglobins: Their Demonstration in Sickle Cell Anemia and Other Hematologic Disorders by Means of Alkali Denaturation", *Blood*, 6: 413.

SMITH, C. H. (1953), "Hypoplastic and Aplastic Anemias of Infancy and Childhood; with a Consideration of the Syndrome of Nonhemolytic Anemia of the Newborn", *J. Pediat.*, 43: 457.

WALSH, R. J., *et alii* (1953), "A Study of Hæmoglobin Values in New South Wales, with Observations on Hæmatocrit and Sedimentation Rate Values", National Health and Medical Research Council, Special Report Series No. 5, Australasian M. Pub. Co., Sydney.

WICKSTER, G. Z. (1952), "Posthemorrhagic Shock in the Newborn", *Am. J. Obst. & Gynec.*, 63: 524.

WIENER, A. S. (1948), "Diagnosis and Treatment of Anemia of the Newborn Caused by Occult Placental Hemorrhage", *Am. J. Obst. & Gynec.*, 56: 717.

A CLINICAL STUDY OF SCRUB TYPHUS IN NORTH QUEENSLAND.[1]

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THIS report is based on a series of 53 patients with scrub typhus studied at the Innisfail Field Station of the Queensland Institute of Medical Research in the period from March, 1953, to November, 1954. They were drawn from a geographical area stretching from Abergowrie, near Ingham, to Cooktown. A previous paper (Carley *et alii*, 1955) discussed strains of *Rickettsia tsutsugamushi* isolated from 27 of this series.

R. tsutsugamushi was isolated from 45 of these patients by mouse inoculation; identification and classification of virulence were carried out as described previously. Proteus agglutination tests were performed on paired sera from all patients, and confirmed the diagnosis in the eight cases in which no strain was isolated.

Clinical Features.

The chief symptoms and signs present, and the frequency with which they were recorded, are shown in Table I.

TABLE I.

Clinical Features Recorded in 53 Cases of Scrub Typhus.

Clinical Feature.	Number of Cases.	Clinical Feature.	Number of Cases.
Headache	48	Lymph-gland enlargement	38
Photophobia	18	Rash	24
Vomiting	15	Eschar	19
Generalized myalgia	10	Conjunctival injection	9
Abdominal pain	9	Abnormal chest signs	7
Backache	9	Albuminuria	8
Cough	14	Splenomegaly	4
Sore throat	7	Hepatic enlargement	5
Frequency of micturition	4	Liver tenderness	13
Dysuria	3		
Neck stiffness	3		
Deafness	1		

Mortality Rate.

The mortality rate was nil, and the general clinical picture was mild in comparison with pre-antibiotic series. Thus Heaslip (1941) recorded one death in 54 cases in the Cairns area, and Mathew (1938) four deaths in 71. This must be associated with the accepted value of the broad spectrum antibiotics.

Features of Onset.

The non-specific symptoms of fever, chills, shivering and sweating were complained of by all patients. Only three had definite rigors. The mode of onset varied; in most cases it was slow, the patient feeling vaguely unwell and feverish in the evenings for some days before his symptoms brought him to hospital. In some cases the onset was sudden, and these were often diagnosed as leptospirosis. There was a striking correlation between the duration of illness before the patient's admission to hospital and the virulence of the causative strain on mouse passage. Thus the average duration from onset to admission to hospital was 4·9 days (standard deviation ± 2·15 days). For virulent strains the average was 3·8 days (standard deviation ± 2·0 days), for intermediate strains 5·4 days (standard deviation ± 2·3 days), for mild strains 5·6 (standard deviation ± 2·0 days). The difference between virulent and mild strains is significant (standard error of difference being 0·7 day, with an observed difference of 1·8 days).

Headache.

Headache was a very prominent symptom, recorded in all except five cases; one other patient denied any headache

[1] Read at a meeting of the Section of Tropical Medicine, Australasian Medical Congress (British Medical Association), Ninth Session, Sydney, August 20 to 27, 1955.

during his primary fever, but complained of it during relapse. Backache, limb pains, or "generalized aches and pains" occurred in 19. Two complained of pain in the back of the neck. One patient noticed a throbbing at the site of her eschar before any general malaise appeared; pain in the regional glands draining the eschar was the presenting complaint in one other case. In nine, abdominal pain was mentioned.

Rash.

A rash appeared on 24 patients, an incidence in agreement with previous Australian series (35 out of 71 in Mathew's cases). In all it was macular, brownish-pink, and maximal on the trunk, and did not itch, desquamate or become petechial. Its duration varied from two to forty-eight hours; the day of onset varied from the third (in one case) and the fourth (in five cases) to the thirteenth. The average time of appearance was 7·3 days, with a standard deviation of ± 2·8 days. In one case a rash appeared only on relapse, on the eleventh day of illness; this patient's primary course of treatment commenced on the third day of illness. In another case a rash appeared on the ninth day, faded on treatment, but reappeared on the sixteenth day during a relapse.

One patient had a confluent pustular eruption on his back, present on his admission to hospital, from which *Staphylococcus aureus* was isolated. The occurrence of similar "pustular dermatitis" was recorded in one wartime series from New Guinea (Williams *et alii*, 1944).

Eschars.

An eschar was found on 19 patients, and a further four had atypical lesions which may have represented eschars modified by chemotherapy. This figure agrees with some previous Australian series — for example, Heaslip (1941) recorded eschars on 17 of 48 patients. Southcott (1947), however, found eschars on 28 of 34 patients from the Bramston Beach outbreak.

The anatomical distribution of the eschars showed the usual centripetal pattern; there were seven on the trunk, two in the axilla, two in the pubic area, two on the scrotum, one in the groin, one on the buttock, one on the forearm, and three on the leg. No patient had more than one eschar.

Only one out of seven aborigines had an eschar, whereas the incidence in white patients was 18 out of 46. The difference is not statistically significant.

There was no correlation between the presence of an eschar and the development of *Proteus* OXK antibodies. Ten of the 19 patients did not yield a significant reaction to the Weil-Felix test.

Respiratory Tract Involvement.

Evidence of involvement of the respiratory tract was not uncommon. Fourteen patients complained of a cough, and seven of these were found to have some abnormality on clinical examination. In six this was limited to scattered râles, but one had the clinical signs and radiological picture of bronchopneumonia. This patient's clinical history is as follows. His temperature chart is shown in Figure I.

A., aged thirty-two years, a full-blood aboriginal, of Yarrabah Mission, near Cairns, fell ill on July 13, 1953, and was admitted to the Mission Hospital on July 15 and transferred to the Cairns Base Hospital on July 20. On examination, he was febrile and had a rapid respiratory rate; there was dullness to percussion, and crepitations were heard at the base of the right lung. He was given penicillin, 250,000 units every four hours; on July 23 he was still febrile, and an X-ray film of the chest revealed bilateral spotty opaque areas involving both lungs, the markings being densest at the base of the left lung. The possibility of acute tuberculosis was considered. On July 28 his spleen was palpable, he had generalized lymph gland enlargement, and his eyes were injected. Chloramphenicol therapy was commenced on August 1, and his temperature fell to normal. A further X-ray film on September 21 was reported as showing some increase in lung markings; the X-ray findings on October 15 were normal.

Six patients complained of sore throat on their admission to hospital; in these six, and in one other, some faucial injection was found on examination.

The respiratory element was less prominent in the present series than in some recorded series; thus Williams *et alii* (1944) found abnormal chest signs in 44% of their patients, and in "practically all the moderately serious or severe cases".

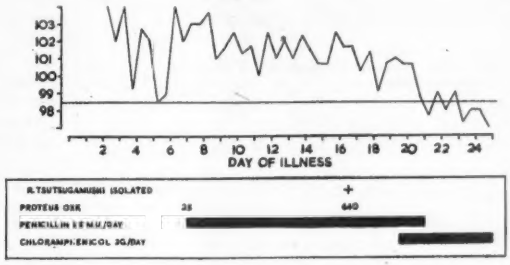

FIGURE I.

Temperature chart of A., aged thirty-two years: scrub typhus treated late, showing typical remittent fever.

Cardio-Vascular Involvement.

Abnormalities of the cardio-vascular system were uncommon. The pulse rate in most cases responded in proportion to the temperature, although in a few it remained low.

One patient developed cardiac failure during treatment; the clinical history was as follows.

B., aged fifty-three years, fell ill on August 28, 1954, with malaise, feverishness and a productive cough. He was admitted to the Innisfail District Hospital on September 3; on examination of the patient, his chest showed a moderate degree of emphysema and some scattered crepitations were heard. A provisional diagnosis of bronchopneumonia was made, and he was treated with penicillin, 100,000 units being given every three hours. On September 8 he was still febrile and his condition had deteriorated; he became mildly cyanosed and orthopnœic, and his cardiac outline appeared enlarged on X-ray examination. By now he had some enlarged axillary glands, and a history of scrub exposure was elicited. After treatment with chloramphenicol his temperature responded, but his condition remained worrying, and he developed œdema of the legs and sacrum. On September 11 he was given digitoxin, 1·2 milligrammes immediately and 0·2 milligramme per day, and his condition improved; he was discharged, well, after a slow convalescence.

Abdominal Pain and Spleen and Liver Involvement.

Abdominal pain was mentioned in nine cases, but in none was it severe. Vomiting occurred in 15, although in several this followed treatment with antibiotics. In one case a poor response to chloramphenicol may have been due to vomiting of the capsules.

Five patients had enlargement of the liver, and tenderness under the right costal margin was recorded in 13 cases. Liver function tests carried out in the following case gave results of interest.

C., aged thirty-three years, an aboriginal, of Yarrabah Mission, was admitted to Cairns Base Hospital on June 1, 1954, with a history of headache, anorexia, photophobia and generalized myalgia of four days' duration. The provisional diagnosis was leptospirosis; on June 8, after forty-eight hours' penicillin therapy, he was still febrile, and the administration of chloramphenicol was commenced, with a prompt response. The diagnosis of scrub typhus was established by the Weil-Felix test, the reciprocal of the OXK titre rising from 0 to 2048. The patient also had antibodies in both sera against *Coxiella burneti*, *Leptospira australis A*, and *L. australis B*.

Liver function tests were performed during his stay in hospital and subsequent weeks by Dr. W. R. Horsfall, of the Cairns Health Laboratory. The results are shown in Table II; they cannot be taken as indicative of liver damage, as the rise in γ-globulin found on paper electrophoresis may well have been due to the antibody response, and could in

TABLE II.
Results of Liver Function Tests on Patient C.

Test.	June 9, 1954.	June 24, 1954.	August 9, 1954.	September 6, 1954.	October 5, 1954.
Serum alkaline phosphatase content (King-Armstrong units) ..	6	7	6·5	14	6·5
Serum bilirubin content (milligrammes per 100 millilitres) ..	<0·5	<0·5	<0·5	<0·5	<0·5
Thymol turbidity (units)	26	18	14	10	8
Thymol flocculation	++	++++	+++	–	–
Zinc sulphate turbidity (units)[1]	10	20	21	16	11
Cephalin-cholesterol flocculation	+++	+	Not estimated.	Not estimated.	Not estimated.
Colloidal gold reaction	+++	+++	+	–	–
Serum protein (grammes *per centum*)	7·4	7·3	7·0	7·4	7·0
Paper electrophoresis	Increase in γ globulin.	Increase in γ globulin.	Not estimated.	Not estimated.	Not estimated.

[1] In the zinc sulphate turbidity test, the technique described by Kunkel was employed, with MacLagan's thymol turbidity standard.

turn have caused the abnormal flocculation and turbidity test results.

Similar liver function test findings in scrub typhus in Japan have been described by Sato *et alii* (1954), who ascribed them to the immunity response.

In four cases splenomegaly was present; in six others tenderness under the left costal margin was recorded, but the spleen could not be felt. This incidence is much lower than in previous Australian series; Mathew (1938) described splenomegaly as "frequent", and Heaslip (1941) recorded it in 12 out of 48 patients.

Urinary Symptoms.

Urinary symptoms were uncommon; five patients complained of dysuria or frequency of micturition. Eight patients had albuminuria and one had biliuria, and in one case a chemical test for blood produced a positive result. The urine was reported as normal on microscopic examination in a number of cases. Blood urea determinations were carried out in two instances; in one of these the content was reported as 68 milligrammes per 100 millilitres. This patient (D.) had persistent albuminuria during his illness; he developed hyperpyrexia early in his illness, and his history is given below. His urinary output appeared adequate.

This single observation is in keeping with the findings of larger war-time series. Williams *et alii* (1944) found a small but consistent rise in the blood urea content between the twelfth and eighteenth days, falling to normal by the beginning of the fourth week.

Mental and Neurological Changes.

The benign clinical picture of the present series can be gauged from the almost complete absence of serious mental or neurological changes. In the New Guinea series quoted above, 231 out of 626 patients had some mental or neurological abnormality, and 90 had nerve deafness. Mathew (1938) recorded mental changes in most of his patients; Clarke (1913) noted deafness in 8% of one group of his "Mossman fever" patients.

Only one patient complained of deafness, which was only transient; two had some impairment of vision; one patient had insomnia; three mentioned neck stiffness. In two of these lumbar puncture produced normal cerebrospinal fluid. One patient developed hyperpyrexia; his history is as follows.

D., aged twenty-five years, of Wangan, a timber worker, was admitted to Innisfail District Hospital on April 4, 1953, with a history of malaise and headache of two days' duration. On his admission to hospital he was febrile, and his axillary and inguinal glands were palpably enlarged. Some hours later he had a violent rigor, his temperature reached 107·8° F., and he had an epileptiform fit. He became violent and excitable, and was sedated with difficulty. Lumbar puncture on April 8 revealed no abnormality. He responded to chloramphenicol, but relapsed, and finally responded to a second course.

Involvement of the Eyes.

Eighteen patients complained of sore eyes and photophobia; conjunctival injection was recorded in nine. One patient (A., mentioned above) was thought to have early keratitis, but his ciliary injection subsided quickly after chemotherapy.

Enlargement of Glands.

Enlargement of lymphatic glands was noted in 38; in some the regional glands draining the site of the eschar were the only ones involved. However, it was more frequent to find generalized lymphadenopathy involving axillary, inguinal, cervical and epitrochlear glands. The enlargement was slow to subside, and in many cases the glands were still palpable months afterwards.

White Cell Counts.

White cell counts were carried out on fourteen patients on occasions from the fourth to the eighteenth day of illness. All lay between 4000 and 9000 per cubic millimetre, with normal differential counts, with three exceptions. A woman, infected with a mild strain, had a count of 3600 per cubic millimetre on the ninth day of illness; one man had a count of 17,650 per cubic millimetre on the ninth day of illness; another (an aboriginal) had a count of 8100 on the tenth day. The films in the two last-mentioned cases were abnormal; the writer is indebted to Dr. Horsfall for the following reports on them.

E. had a white cell count of 17,650 per cubic millimetre. The differential count was as follows: neutrophile cells 22%, lymphocytes 77%, monocytes 1%. Many of the lymphocytes had dark blue cytoplasm, rather similar to plasma cells, but smaller. The cells were not typical glandular fever cells, but could be a small variety of that type.

F. had a white cell count of 8100 per cubic millimetre. The differential count was as follows: neutrophile cells 47%, lymphocytes 29%, monocytes 6%, Turck cells 2% and atypical lymphocytes 16%.

In the latter case the Paul-Bunnell test produced a positive reaction at a titre of 1/14 (unabsorbed).

Williams *et alii* (1944) wrote as follows:

> The lymphocytes appear to play a more important part in typhus than do the other leucocytes. . . . In nearly all non-fatal cases there was an increase in lymphocytes just before the patient started to show clinical improvement.

The Disease in Children.

Unwin (1935) wrote as follows:

> The disease occurs in children as well as in adults, but in the former as a rule is of a much milder type.

Three children are included in this series, two white boys, both aged five years, and an aboriginal boy, aged seven years, and their clinical courses support Unwin's statement. The aboriginal was treated at an outlying hospital, and his clinical records are scanty; however, his illness lasted eleven days, and was terminated by chloramphenicol. The white boys were both treated at Innisfail District Hospital; neither had an eschar; one developed a fleeting rash; both responded to chloramphenicol, but one relapsed and required a second course. In each case the causative strain of *Rickettsia tsutsugamushi* was isolated; in two it was of mild virulence; in the third the strain

was intermediate in early passage but became virulent in later passages.

Influence of Strain Virulence on Clinical Features.

R. tsutsugamushi was isolated from 45 of these patients, and the strains were investigated by mouse passage and cross-immunity reactions at the Queensland Institute of Medical Research, Brisbane. The techniques used, and the criteria by which strains were classified as mild, intermediate, or virulent, have been described in a previous paper (Carley *et alii*, 1955).

The virulence of the strain isolated from the patient can be correlated with certain features of the clinical course. Thus the duration of illness from onset to the patient's admission to hospital was shorter in patients infected with virulent strains (this has been discussed above). Individual patients who had a stormy course (A., B. and D., whose histories have been given) were infected with virulent strains. Patients whose response to chloramphenicol appeared suboptimal were more often infected with virulent strains (this will be discussed below).

Detailed analysis of individual clinical features is handicapped by the small numbers involved. The most frequent signs and symptoms (eschar, rash, lymphadenopathy *et cetera*) did not show any association with strain virulence. Albuminuria was recorded in only one of 17 patients infected with mild strains, in one of six infected with intermediate strains, and in five of 22 infected with virulent strains. The differences are not significant.

It is probable that the early suppression of disease with antibiotics prevented a more obvious relation between clinical severity and strain virulence.

Course of Illness.

The incubation period of scrub typhus in North Queensland is known to approximate to twelve days (Andrew, 1945). Southcott (1947) reached an average figure of 13·06 ± 1·89 days in 70 cases in the Bramston Beach epidemic.

There were only five patients in the present series whose exposure was brief enough to allow a close estimate of the incubation period. Their histories were as follows: (i) A woman, who spent twenty minutes sitting in grass at Bramston Beach, noticed pain at the site of an eschar eight days later. (ii) and (iii) Two men, who spent a weekend cutting timber at Bramston Beach, fell ill two days apart, with incubation periods of nine to ten days and eleven to twelve days respectively. (iv) A boy fell ill eleven days after an orchid-hunting expedition at Flying Fish Point. (v) Another boy fell ill ten days after a scrub walk at Flying Fish Point.

The total duration of fever reflects the effects of treatment; the figures for the various groups are shown in Table III. The average duration for 50 patients for whom figures were available was 10·3 days, with a standard deviation of 4·2 days. Five patients, who did not receive an effective antibiotic, had an average duration of 14·2 days, with a standard deviation of 3·2 days.

TABLE III.

Patient Group.	Number of Patients.	Mean Duration of Primary Fever. (Days.)	Standard Deviation.
Patients not treated with an effective antibiotic	5	14·2	3·2
Patients treated with broad-spectrum antibiotic:			
Virulent strain infections ..	19	9·9	5·0
Intermediate strain infections ..	6	9·3	3·6
Mild strain infections	15	10·0	2·5
Strain not isolated	5	10·4	5·1

There was no significant difference in average duration of fever in patients from whom virulent, intermediate and mild strains were isolated.

The temperature chart was characteristically remittent, with pronounced daily swings (see Figure I). In many cases this tendency may have been enhanced by aspirin and other antipyretics. Sayen *et alii* (1946) mention that they came to look upon an irregular "spiking" type of temperature chart with double daily rises as typical of scrub typhus. This feature, while it was seen in several of the present series, did not occur sufficiently often to have any diagnostic significance.

The highest temperature recorded was 107·8° F. (D., mentioned above). In only seven cases was a temperature of 102° F. or higher not recorded at least once during the illness. There was no definite correlation between the height of the temperature recorded and the virulence of the causative strain.

Nine patients relapsed after treatment; their cases are discussed in detail below.

Treatment.

Forty-five patients were treated with chloramphenicol, two with tetracycline, and one with chlortetracycline.

The total dosage of chloramphenicol varied from five to 22 grammes, and several regimes were employed. Five patients were given six grammes in twenty-four hours; seven received six grammes in thirty-six hours; one received nine grammes in forty-eight hours; five received 1·5 grammes per day for some days after loading doses of one to three grammes; one received one gramme per day for four days after an initial dose of one gramme. The remainder received either two or three grammes per day until the temperature fell to normal, and in most cases for twenty-four to forty-eight hours longer; a number of these received an initial dose of one to three grammes.

The overall results were very satisfactory. The average duration of fever after the first dose of antibiotic was 45·5 hours, with a standard deviation of 34·6 hours. In the estimation of this average, patients were omitted who did not respond fully to the antibiotic and who were still febrile when treatment was stopped. Prezyna *et alii* (1954) found an average duration of forty hours after chloramphenicol in their Pescadores series.

Durations of fever after chloramphenicol are analysed in groups of strain virulence in Table IV. There is no statistically significant correlation between the virulence and the speed of response.

Prezyna *et alii* (1954) found that patients treated late in the course of their illness responded more quickly than those treated early. A similar tendency is obvious in the present series. Thus patients treated on the eighth day or earlier had an average febrile period of fifty-seven hours or, if three extreme values are excluded, forty-six hours. The patients treated on the ninth day or later had an average duration of fever of twenty-seven hours. However, neither of the groups is homogeneous as regards strain virulence or antibiotic dosage, and calculation of the correlation coefficient for these two figures—day on which treatment is commenced and duration after treatment—suggests that this difference is not significant (correlation coefficient −0·27, with a standard error of 0·16).

Seven patients showed a less satisfactory response to treatment than was expected. Their details are summarized in Table V. It can be seen that in five of the seven cases the illnesses were due to virulent strains, and in the two cases due to mild strains one patient had vomited the capsules and may not have retained an adequate dose.

Of the five patients whose illness was due to virulent strains, four received what would be accepted as adequate dosage. The other was given 1·5 grammes per day, about 20 milligrammes per kilogram, which was probably inadequate.

The poor response of one of the patients given tetracycline is of interest. Her condition improved on treat-

TABLE IV.

Relation between Duration of Fever after the Primary Course of Chloramphenicol, and the Virulence of the Strain Isolated.

Strains.	Number of Patients with Duration of Fever of—					
	0 to 20 Hours.	21 to 40 Hours.	41 to 60 Hours.	61 to 80 Hours.	More than 80 Hours.	Total.
Mild strains	2	8	1	1	3	15
Intermediate strains	2	1	2	0	1	6
Virulent strains	2	6	4	3	4	19
Total	6	15	7	4	8	40

ment, but she remained febrile for over twelve days. The other patient given tetracycline responded in twenty-two hours. Further work is needed to assess the value of this antibiotic.

Several papers have mentioned the occurrence of cases of scrub typhus responding slowly to treatment; for example, Prezyna *et alii* (1954) found that 40% of their patients who were given chloramphenicol remained febrile over forty hours, up to 104 hours. Bailey *et alii* (1951) describes one patient who was febrile ninety-six hours after receiving six grammes of chloramphenicol. The explanation of such cases is not clear.

The course of scrub typhus treated late is shown in Figure I; a typical rapid response is shown in Figure II, and Figure III shows the chart of patient I., who responded poorly to two courses of chloramphenicol.

Relapses.

Nineteen patients had at least one temperature recording above 99° F. after the primary response to treatment. There was also the patient, discussed above, who did not respond to the first course of antibiotic and who was given a second. In 10 cases of the 19 the rise in temperature was restricted to a single reading or lasted less than one day, and is considered of doubtful significance. It is of interest that similar short, doubtful relapses were described in patients in Malaya by Bailey *et alii* (1951).

The mechanism underlying relapse in scrub typhus after antibiotic suppression has been studied in detail by Smadel and his colleagues (Smadel *et alii*, 1950). They recorded 62% relapses in 34 patients treated with chloramphenicol before the fourth day of illness, 37% in 27 patients treated after the fourth day (on the average, the sixth day), and none in patients untreated or given paraaminobenzoic acid. An inverse relation between relapses and the development of a significant OXK titre was found, but did not reach statistical significance; thus 71% of those with the highest relapse rate were found to have antibodies, compared with all the untreated, relapse-free series.

Smadel (1954) put forward an hypothesis regarding relapses, based upon the observations that the specific antibiotics are rickettsiostatic rather than rickettsiocidal, and that a single large dose of antibiotic suppressed disease for five or six days, and the general experience that the untreated, uncomplicated disease lasts on the average fourteen days. He assumed that "for some unknown reason in the typhus fevers it takes about two weeks of illness before these defences (i.e. the immunologic defences of the patient) are completely mobilized".

It is of interest to examine the present series with these findings in mind. The details of the nine patients with relapses are summarized in Table VI.

One was treated with chloramphenicol, in a dosage of two grammes per day, the administration having commenced on the third day of illness. His temperature fell promptly to normal, but on the seventh day, while the antibiotic was still being administered, it rose again, and he was febrile for four days. This breaking through of the antibiotic cover is puzzling; it is possible that the dose was too low to maintain suppression.

Three patients had relapses lasting three, two, and two days respectively, subsiding without further treatment. In one of these, rickettsæmia was demonstrated during relapse. Treatment in the primary illness was commenced on the fourth, sixth and ninth days respectively. In two cases the strains were isolated; one was classified as mild and one as intermediate. Two of the three patients had no OXK antibodies; the third developed a titre of 1/1280.

Five patients received a second course of antibiotic, and in two cases rickettsæmia was demonstrated during relapse. Three were infected with virulent strains, one with an intermediate strain, and one with a mild strain. Two, the patients from whom the mild and intermediate

TABLE V.

Details of Patients who Showed a Poor Response to Treatment.

Patient.	Sex.	Strain Virulence.	Highest OXK Titre (as Reciprocal).	Antibiotic Treatment and Dosage in Grammes.	Day of Illness Treatment Commenced.	Day Treatment Ceased.	Duration of Fever after Treatment. (Hours.)	Remarks.
G.	M.	Virulent.	80	Chloramphenicol, 1·5 grammes per day.	5	14	168	
H.	M.	Virulent.	0	Chloramphenicol, 1·0 gramme *statim*, 3·0 grammes per day.	6	13	136	
I.	M.	Virulent.	128	Chloramphenicol, 6·0 grammes in 36 hours.	(i) 6 (ii) 10	(i) 7 (ii) 11	(i) 186 (ii) 90	
J.	F.	Virulent.	0	Chloramphenicol, 9·5 grammes in 39 hours.	6	8	160	
K.	M.	Mild.	0	"Chloromycetin Palmitate", 1·0 gramme *statim*, 2·0 grammes per day.	8	14	140	History of recent exacerbation of peptic ulcer—given paediatric suspension.
L.	F.	Virulent.	32	Tetracycline, 1·0 gramme *statim*, 3·0 grammes per day (reduced later to 1·5 grammes per day).	8	16	300	
M.	F.	Mild.	128	Chloramphenicol, 1·0 gramme *statim*, 3·0 grammes per day.	4	Not known.	>48	Vomited capsules; left hospital still febrile.

strains were isolated, were OXK-negative. Treatment of the primary illness was commenced on the third, fourth, sixth, sixth, and ninth days respectively.

Therefore, of three patients whose treatment was commenced on the third day, two relapsed. Of four treated on the fourth day, two relapsed. None of the four treated on the fifth day relapsed, but three relapsed of the six treated on the sixth day.

No patient treated after the ninth day of illness relapsed.

Five of those with relapses were OXK-negative; this is a higher incidence than was found in the series as a whole. However, the difference is not significant.

Four patients with relapses were infected with virulent strains, two with intermediate strains, and two with mild strains. This does not differ significantly from the overall incidence. It may be noted that all patients infected with mild or intermediate strains and showing relapses were OXK-negative.

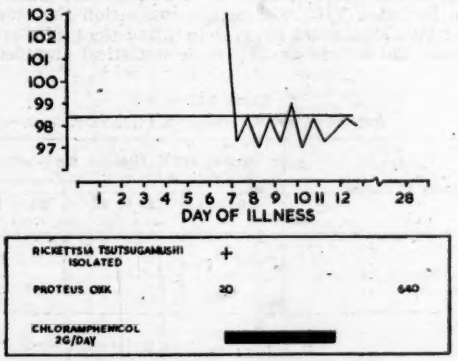

FIGURE II.

Temperature chart of V., aged eighteen years, showing rapid response in scrub typhus treated with chloramphenicol.

The five-day interval between antibiotic therapy and relapse, described by Smadel (1953), is not evident in the present series. The intervals between the cessation of treatment and relapse were twelve days in one, and eleven in another; one patient relapsed immediately the administration of the antibiotic was stopped, another relapsed while chloramphenicol was still being administered, and in the remainder the intervals were one, two, three, four and four days respectively. It must be pointed out, however, that these patients are not strictly comparable with the American series, as the dosage varied. None received the single large dose used by Smadel, and most received treatment for a longer period at a lower rate per day (see Table VI). This may explain the more variable periods of suppression in the North Queensland patients.

The temperature appeared to respond more quickly to the second course of antibiotic for the four patients for whom exact figures are available (see Table VI). Three received a similar course in their relapse, but one patient was given a higher dose of chloramphenicol in relapse.

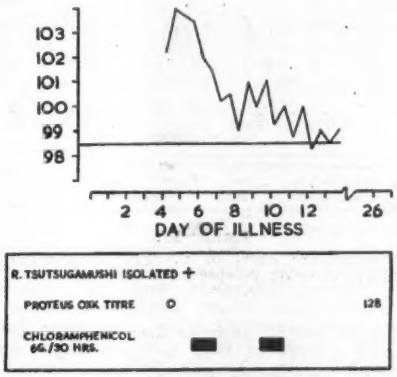

FIGURE III.

Temperature chart of I, aged thirty-three years, showing an incomplete response to chloramphenicol, and a poor or doubtful response to a second course.

There is some evidence that the response to treatment is more rapid the later it is instituted (Prezyna *et alii*, 1954). The evidence for this is discussed above; it may account for the difference between the primary illness and relapse.

The temperature chart of a patient with a typical relapse is shown in Figure IV.

It would seem justifiable to state that the administration of a total of six grammes of chloramphenicol, in divided doses over twenty-four to forty-eight hours, is adequate

TABLE VI.

Details of Patients who Relapsed after Responding to Antibiotic Treatment.

Patient.	Strain Virulence.	Highest Proteus OXK Titre (as Reciprocal).	Rickettsia Isolated.		Primary Fever.			Relapse.		
			In Primary Fever.	In Relapse.	Day of Illness Treatment Commenced.	Treatment with Chloramphenicol. (Grammes.)	Duration of Fever after Treatment.	Day of Illness of Relapse.	Treatment with Chloramphenicol. (Grammes.)	Duration of Fever after Treatment.
D.	Virulent.	160	+		6	6·0 in 24 hours.	68 hours.	10	6·0 in 24 hours.	42 hours.
N.	Mild.	0	+		6	5·0 in 48 hours.	40 hours.	20	6·0 in 24 hours.	12 hours.
O.	Intermediate.	0	+	+	9	7·0 in 48 hours.	70 hours.	12	7·0 in 48 hours.	24 hours.
P.	Virulent.	1024	+		3	6·0 in 96 hours.	52 hours.	11	6·0 in 96 hours.	Not known.
Q. (child)	Virulent.	512	+	+	4	5·5 in 120 hours.	52 hours.	9	5·0 in 96 hours.	20 hours.
R.	Strain not isolated.	1280			4	6·0 in 24 hours.	36 hours.	9	Nil.	—
S.	Mild.	0		+	6	7·0 in 72 hours.	32 hours.	20	Nil.	—
T.	Intermediate.	0	+		9	6·0 in 36 hours.	24 hours.	13	Nil.	—
U.	Virulent.	0	+		3	16·0 in 8 days.	38 hours.	7	Primary course continued through relapse.	—

treatment for most patients with scrub typhus in North Queensland, provided that the possibility of relapse is realized. Patients should be kept under observation, preferably in hospital, for at least seven days after their temperature has fallen to normal.

Proteus OXK Agglutination.

Sera collected from all patients on admission to hospital and at least once during convalescence were tested for antibodies against *Proteus* OXK, *Proteus* OX19, the Australian serotypes of leptospiræ, *Coxiella burneti*, *R. mooseri*, *R. akari*, *Brucella abortus*, *Salmonella typhosa*, *S. paratyphi*, and *S. schottmülleri*. Only the *Proteus* OXK results were of significance.

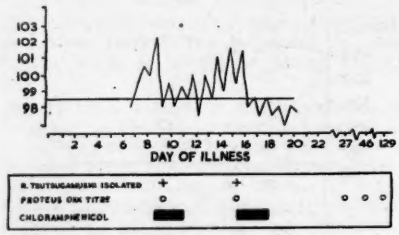

FIGURE IV.

Temperature chart of O, aged thirty-seven years, showing relapse after first course of chloramphenicol.

Seventeen of the 53 patients had no OXK antibodies; nine reached a titre of 1/20 to 1/40, which would not be considered significant, and 27 had a titre of 1/80 or greater. Of the 36 cases in which antibodies were present, in eight the diagnosis was made only by the Weil-Felix test, as mouse inoculation was not performed in seven and failed in one. The more accurate proportion of OXK-negative cases is therefore 17 out of 45. OXK-negative cases that were not investigated by mouse inoculation remained undiagnosed and were not included in the series.

The occurrence of cases of scrub typhus in which OXK antibodies to a significant titre are not developed is well recognized. Thus Mathew (1938) had three typical cases (two fatal) in which the titre did not exceed 1/50; Williams *et alii* (1944) found that in 8% of their series the OXK titre did not exceed 1/25; Andrew (1945) had two patients in 21 whose titre did not exceed 1/80. Prezyna *et alii* (1954) recognized one OXK-negative case in the Pescadores.

However, there is little in the North Queensland literature from pre-antibiotic days to lead one to expect the high incidence of OXK-negative cases reported here. It may be considered that, as the diagnosis depended on the Weil-Felix reaction, OXK-negative cases would have remained undiagnosed. However, Heaslip (1941) investigated a number of patients by mouse inoculation and found only two out of 54 without OXK antibodies, although in another nine the titre did not exceed 1/40.

The factors that may have been responsible for this high incidence of OXK-negative cases have been discussed in a previous paper (Carley *et alii*, 1955). As the present series includes more cases, it is possible to carry the analysis a little further. It must again be pointed out that in most cases a single convalescent serum was tested; it is therefore possible that OXK antibodies may have developed to a higher titre than that recorded. Serum was taken at close intervals from several OXK-negative patients, and it is clear that this factor alone cannot account for the high incidence of OXK-negative cases.

It can be stated that no statistically significant relationship can as yet be demonstrated between the OXK titre developed and the race or age of the patient, the virulence of the infecting strain, previous infection with scrub typhus, the day of illness on which treatment was commenced, or the total number of febrile days. However, in some cases an apparent relationship approaches statistical significance. Each of these factors will be discussed.

Race.

Three of seven aborigines were OXK-negative and another had a titre of 1/20. The others, however, had titres of 1/512, 1/640 and 1/2048. Four patients with absent or low OXK titres were of Mediterranean ancestry, as were three with diagnostic levels. These incidences do not differ significantly from the distribution of the whole series.

Age.

The average age of 17 OXK-negative patients was 33·8 years, that of 27 with an OXK titre greater than 1/40 was 32·9 years, and that of nine with an OXK titre between 1/20 and 1/40 was 28·5 years. The differences are not significant.

Strain Virulence.

The distribution of OXK titres in patients from whom strains of the three grades of virulence were isolated is shown in Table VII. There is a suggestion that virulent strains give significant titres more often than mild strains. However, the figures do not reach statistical significance.

TABLE VII.

Relation of Strain Virulence to OXK Titre.

Strain Virulence.	Proteus OXK Titre (as Reciprocal).		
	0	20 to 40	80 or More.
Mild	9	3	5
Intermediate	2	0	4
Virulent	6	4	12

Previous Infection.

Smadel *et alii* (1952) found lower OXK titres in human volunteers having their second attack of scrub typhus. One patient in the present series had suffered from scrub typhus in New Guinea twelve years before his recent attack. His OXK response was negative in the present illness; his treatment with chloramphenicol commenced on the third day of illness. Many of the series had lived for long periods in scrub typhus areas and had histories of "coastal fever", but none had previous proven attacks of scrub typhus, and in no case did hospital records of previous illness suggest scrub typhus.

Treatment.

The work of Smadel and his colleagues (Smadel, 1954) has demonstrated some interrelation between the OXK titre developed and the day of illness on which a patient with scrub typhus is treated with an effective antibiotic. Smadel wrote as follows:

> If the drug (chloramphenicol) is used prophylactically to obtain clinical suppression of disease the antibody levels remain low. On the other hand, in patients who are treated after the latter part of the first week of illness the levels approximate those in untreated patients who run the full course of two weeks of fever.

In the present series three patients were treated on the third day of illness; all were infected with virulent strains, and the OXK titres reached were 0, 1/32 and 1/1024. Fourteen patients infected with virulent or intermediate strains were treated on the fourth to seventh days, and two of these were OXK-negative. Six patients infected with mild strains were treated on the fourth to seventh day; all were OXK-negative, except one who vomited the chloramphenicol and remained febrile for some days. She developed an OXK titre of 1/128.

If, therefore, antibiotic suppression of antibody formation contributes to the proportion of OXK-negative patients, it would appear to affect mainly infections with mild strains. This is further analysed in Table VIII; of 10

patients infected with mild strains and treated before the ninth day, only two developed OXK antibodies, but of six treated after the ninth day, all developed OXK antibodies. The difference appears to be statistically significant, but since three of those treated late and accepted as OXK-positive, developed titres of only 1/32, 1/40 and 1/40 respectively, the result could be fortuitous.

Smadel (1954) has shown that the Weil-Felix reaction may also be influenced by the stage at which treatment is given, not in the maximal titre obtained, but in the rate of attainment of that titre. One patient in the present series had no antibodies at thirty-one days, and a titre of 1/128 at forty-nine days; she received chloramphenicol. Another, however, who had no antibodies at twenty-nine days, and a titre of 1/20 at fifty days, did not receive a broad spectrum antibiotic. These were the only recognized instances of a delayed rise in antibody in the present series.

Obviously no definite deductions can be drawn as yet, but the following points may be made:

TABLE VIII.

Relation between Strain Virulence, Proteus OXK Titre and Day on which Treatment was Commenced.

Treatment Commenced.	Mild Strains.[1]		Virulent and Intermediate Strains.[2]		Total.
	OXK-Positive.[3]	OXK-Negative.	OXK-Positive.[1]	OXK-Negative.	
Before ninth day	2	8	15	4	29
Ninth day or later	6	0	3	4	13
Total ..	8	8	18	8	42

[1] For mild strains, $P<0{\cdot}01$.

[2] For virulens and intermediate strains, $P<0{\cdot}05$.

[3] OXK-positive in this table includes all patients with an OXK titre of 1/32 or greater.

1. For the practical purpose of diagnosing scrub typhus in North Queensland the Weil-Felix reaction can be expected to detect only a little more than half the cases that occur.

2. While the high incidence of OXK-negative cases may be due to factors connected with the stage at which treatment is commenced, and the virulence of the strain, these factors cannot account for them all, as patients infected with virulent strains, untreated with an effective antibiotic, may remain OXK-negative.

Conclusion.

Scrub typhus has been diagnosed in North Queensland since 1935 and forms a recognizable entity in accounts of "coastal fever" very much earlier (Clarke, 1913). Work carried out since 1951 by the Queensland Institute of Medical Research has demonstrated a number of features of interest, notably a high proportion of strains that are not fatal to mice, and the failure of about half the patients to develop agglutinins to *Proteus* OXK to a diagnostic titre. The present paper shows that a series of patients, including this proportion who were OXK-negative, displayed clinical features compatible with those described by earlier authors, and that the response of the North Queensland strains to antibiotics resembles that described by overseas workers, with a similar tendency to relapse in patients treated during the first week of fever.

Summary.

1. Fifty-three cases of scrub typhus in North Queensland are reported; 45 were diagnosed by the isolation of *R. tsutsugamushi* by mouse inoculation and eight by the Weil-Felix test.

2. The clinical picture was milder than that described in pre-antibiotic Queensland series, although several patients had severe illnesses. Lymph-gland enlargement, rash and eschar were the commonest findings on physical examination.

3. Several points of correlation could be demonstrated between the clinical picture and the virulence of the causative organism to mice.

4. The course of the disease reflected the influence of treatment, especially in the total duration of fever. A close estimate of the incubation period was possible in five patients.

5. Forty-six patients were treated with chloramphenicol and three with other broad-spectrum antibiotics. The results were satisfactory; in seven cases the response was less rapid than expected, and their clinical features are analysed. Nine patients relapsed after responding to treatment.

6. Seventeen patients did not develop agglutinins against *Proteus* OXK, and in seven others a diagnostic titre was not reached. The factors that may have influenced this are discussed, and some evidence is presented that mild strain infections, treated with an effective antibiotic early in the illness, are more often OXK-negative.

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References.

ANDREW, R. (1945), "A Note on the Incubation Period of Scrub Typhus and its Correlation with Clinical Severity", M. J. AUSTRALIA, 2: 335.

BAILEY, C. A., LEY, H. L., DIERCKS, F. H., LEWTHWAITE, R., and SMADEL, J. E. (1951), "Treatment of Scrub Typhus: Evaluation of Chloramphenicol, Aureomycin, Terramycin, and Para-amino Benzoic Acid", *Antibiotics & Chemother.*, 1: 16.

CARLEY, J. G., DOHERTY, R. L., DERRICK, E. H., POPE, J. H., EMANUEL, M. L., and ROSS, C. J. (1955), "The Investigation of Fevers in North Queensland by Mouse Inoculation, with Particular Reference to Scrub Typhus", *Australasian Ann. Med.*, 4: 91.

CLARKE, P. S. (1913), "Report on 'Mossman Fever'", Queensland: Annual Report of the Commissioner of Public Health to 30th June, 1913: 32.

HEASLIP, W. G. (1941), "Tsutsugamushi Fever in North Queensland, Australia", M. J. AUSTRALIA, 1: 380.

MATHEW, R. Y. (1938), "Endemic Typhus in North Queensland", M. J. AUSTRALIA, 2: 371.

PREZYNA, A. P., CHANG TEH-LING, WANG TSU-LIN, DOUGHERTY, W. J., and BOND, H. B. (1954), "Treatment of Scrub Typhus in the Pescadores Islands with Chloramphenicol, Aureomycin, and Terramycin", *Am. J. Trop. Med.*, 3: 608.

SATO, K. (1954), "On the Results of Some Liver Function Tests in Tsutsugamushi Disease", *Acta med. et biol. Niigata*, 2: 397; abstracted in *Trop. Dis. Bull.* (1955), 52: 30.

SAYEN, J. J., POND, H. S., FORRESTER, J. S., and WOOD, F. C. (1946), "Scrub Typhus in Assam and Burma: A Clinical Study of 616 Cases", *Medicine*, 25: 155.

SMADEL, J. E. (1954), "Influence of Antibiotics on Immunologic Responses in Scrub Typhus", *Am. J. Med.*, 17: 246.

SMADEL, J. E., BAILEY, C. A., and DIERCKS, F. H. (1950), "Chloramphenicol (Chloromycetin) in the Chemoprophylaxis of Scrub Typhus (Tsutsugamushi Disease), IV. Relapses of Scrub Typhus in Treated Volunteers and their Prevention", *Am. J. Hyg.*, 51: 229.

SMADEL, J. E., LEY, H. L., JUNIOR, DIERCKS, F. H., and CAMERON, J. A. P. (1952), "Persistence of Rickettsia Tsutsugamushi in Tissues of Patients Recovered from Scrub Typhus", *Am. J. Hyg.*, 56: 294.

SOUTHCOTT, R. V. (1947), "Observations on the Epidemiology of Tsutsugamushi Disease in North Queensland", M. J. AUSTRALIA, 2: 441.

UNWIN, M. L. (1935), "'Coastal Fever' and Endemic Tropical Typhus in North Queensland: Recent Investigation, Clinical and Laboratory Findings", M. J. AUSTRALIA, 2: 303.

WILLIAMS, S. W., SINCLAIR, A. J. M., and JACKSON, A. V. (1944), "Mite-borne (Scrub) Typhus in Papua and the Mandated Territory of New Guinea: Report of 626 Cases", M. J. AUSTRALIA, 2: 525.

SOME FINDINGS IN THE ADRENAL GLANDS IN UNEXPLAINED OR UNEXPECTED DEATH.

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Hæmorrhage.

THE most common and the most important pathological condition found in the adrenals in unexpected or unexplained death is hæmorrhage. Massive bilateral adrenal hæmorrhage is usually associated with fulminating meningococcal septicæmia—a condition which may kill with great speed. This is very important clinically, especially in children, particularly when it is realized that a child may be put to bed apparently well at night, only to be found dead in bed in the morning, having succumbed during the night to overwhelming meningococcal septicæmia. Most of our cases have occurred in infants and young children, but the condition has also been encountered in adults, even in the elderly, simply found dead in bed.

In 320 sudden or unexpected deaths in infants and children aged up to fourteen years, the Waterhouse-Friderichsen syndrome was found 25 times. In some cases of meningococcal septicæmia no hæmorrhage into the adrenals is found on macroscopic examination, but there is œdema of the tissues in the surrounding area. This may be a useful guide to the presence of associated septicæmia.

In some cases of meningococcal septicæmia the purpuric hæmorrhages in the skin may be so large and so like traumatic bruising that the appearances may suggest that the subject has died from violence. In other instances the rapid onset and the intensity of the symptoms, with much vomiting, may lead to a suspicion of death from poisoning.

At autopsy bilateral adrenal hæmorrhage is not likely to be overlooked. In infants the inner zone of the adrenal cortex is highly vascular, and this may be mistaken for hæmorrhage, especially on microscopic examination. Bilateral adrenal hæmorrhage is sometimes found in infants who die shortly after birth, in whom it appears to be the result of trauma to the very vascular cortex.

Adrenal hæmorrhages may occur as the result of trauma in accidents (run-over cases and such like). In the subjects of traumatic hæmorrhage examined by us, there were other serious injuries such as rupture of the liver, rupture of the kidney *et cetera* to account for death.

Atrophy (Idiopathic).

Adrenal atrophy may be brought about in various ways, but no cause was found in the cases mentioned below. Atrophy of the adrenals is one of the conditions which needs to be kept in mind during the search at autopsy for the cause of an unexplained death. Of five cases in which Addison's disease was found as the cause of death in routine coroner's autopsies, four were due to idiopathic atrophy, one was due to tuberculosis. Here is an example:

A nursing sister, aged twenty-seven years, became ill during the night, with the sudden onset of colicky abdominal pain, vomiting and diarrhœa. She was examined by her doctor, who considered that she was suffering from gastro-enteritis. With treatment the diarrhœa subsided in a few hours, and the vomiting gradually decreased over the next thirty-six hours, when she was able to take a little solid food. Forty-eight hours after the onset her general condition was improving, although she was still very exhausted. Her mental condition was poor, and her doctor believed that the patient had good reason to be greatly disturbed mentally and did not wish to get well. Four days after the onset of this illness the patient lapsed into a semi-coma, and it was impossible to get her to take fluids. Within a few hours her condition rapidly deteriorated, and she died before her admission to hospital could be arranged. It was said that one year before this she had suffered from a "stomach complaint". It was thought that this girl may have died from poisoning, and her death was reported to the coroner.

Post-mortem examination revealed nothing very characteristic externally, apart from some freckling of the face. The internal organs all appeared healthy apart from the adrenal glands, which were smaller than normal. Microscopic examination showed that there was very little normal tissue present; most of the tissue was fibrous, scattered remnants of the adrenal being embedded in the fibrous tissue.

Adrenal atrophy was also found to be the cause of a maternal death investigated at the request of the Consultative Council on Maternal Mortality. This case has been fully reported by Dr. Bruce Anderson, and full clinical details will be found in that report.

The subject, a married woman having her first child, suffered from attacks of vomiting and diarrhœa during her pregnancy. She was carefully managed and came into labour in hospital at term. The labour pains passed off, so she was discharged from hospital. She then had an attack of vomiting which lasted for twenty-four hours, and was placed in hospital again. The membranes were ruptured. Labour was induced and completed by Cæsarean section. During pregnancy her blood pressure had not exceeded 100 millimetres of mercury, systolic, and 60 millimetres, diastolic. After delivery a shock-like state developed, and consciousness did not return for four hours. The woman then lapsed into coma and after a convulsive seizure died, despite resuscitative measures. Post-mortem examination revealed very black areolæ. On internal examination no trace of the right adrenal was found. Some tissue on the left side, which was thought to be the remains of the adrenal, on microscopic investigation was found to contain remnants of the gland embedded in fibrous tissue. In retrospect her clinical history then became clear.

The adrenals at autopsy may appear to be adequate in amount; but unless they are subjected to microscopic investigation adrenal atrophy may be overlooked.

Tuberculosis.

Tuberculosis of the adrenals as a cause of unexplained or unexpected death is in our experience uncommon, but nevertheless it is of medico-legal interest.

For example, a man, previously healthy, had recently married a woman who was not acceptable to his family. Shortly afterwards his health began to fail. He began to lose weight and suffered from attacks of intermittent diarrhœa. He was examined by a physician, who suspected that he might be suffering from Addison's disease; but clinical examination revealed insufficient evidence to enable a firm diagnosis to be made. He died shortly after coming under medical observation. In view of the history that he had suffered attacks of vomiting and diarrhœa, and that his health had begun to fail shortly after his unacceptable marriage, the possibility of death from poisoning was considered. Consequently the matter was referred to the coroner. Post-mortem examination showed the cause of death to be caseating tuberculosis of the adrenals with gross destruction of the glands.

Attacks of vomiting and diarrhœa may be evident in adrenal insufficiency. Because of the similarity of some of the clinical features to those of some forms of poisoning —for example, homicidal poisoning or acute food poisoning —from time to time these cases are referred to coroners for investigation.

Tumours (Pheochromocytoma).

Of the various tumours of the adrenals, primary or secondary, unilateral or bilateral, found at autopsy, pheochromocytoma, although not common, is of some medico-legal significance.

For example, Mrs. B., aged fifty-two years, had no previous medical history, apart from the fact that ten days before her death she had visited her doctor complaining of indigestion. Examination at that time showed some tachycardia, and a systolic blood pressure of 170 millimetres of mercury. On the day of her death she developed sudden

continuous epigastric pain and dry retching. This lasted for eight hours, when she was examined by another doctor, who found her to have vague tenderness in the upper part of the abdomen and occasional extrasystoles. Clinical examination also revealed the presence of a few moist sounds in the lungs. Mrs. B. was considered to be suffering from gastro-enteritis, and treatment was ordered accordingly. Half an hour afterwards she died suddenly. As her death was entirely unexpected, and as the previous examination had revealed no adequate cause for sudden death, the matter was reported to the coroner.

Post-mortem examination revealed gross pulmonary œdema, and a tumour of the left adrenal gland two inches in diameter, which proved to be a phœochromocytoma with large irregular or polyhedral tumour cells.

Gonzales mentions a more rapidly fatal case of hyperadrenalism in a well-developed white man, aged thirty-two years, who suddenly collapsed with some abdominal pain and died one hour later. He had not previously complained of any symptoms. Autopsy disclosed a pheochromocytoma of the right adrenal gland weighing 30 grammes, and this when assayed contained 300 milligrammes of adrenaline.

Pheochromocytoma was also found to be the underlying cause of death in the following case of "death on the table".

Mrs. K., aged forty-six years, had been examined by her doctor on many occasions during the two and a half years preceding her death. Her chief complaint was of "heart turns". She had complained that in one of these attacks she felt as though the circulation was cut off in her hands, which became stiff and grey in colour. She was considered to be "nervy". The only positive finding on examination was that her blood pressure was 200 millimetres of mercury, systolic, and 130 millimetres, diastolic. On three separate occasions prior to her death her blood pressure was found to be high, the systolic pressure varying between 200 and 220 millimetres of mercury. Mrs. K. then went to an osteopath, who, she said, pushed a displaced bone in her vertebral column back into position; but this failed to cure her various upsets. She was eventually found to have a large fibroid tumour of the uterus, for which operation was undertaken. Anæsthesia was induced with "Pentothal", 0·3 gramme, and "Tubarine", 20 milligrammes. Intubation was carried out without difficulty and anæsthesia was maintained with nitrous oxide and oxygen. Just after the peritoneum was opened considerable cyanosis developed, and a bubbling noise was heard in the endotracheal tube. Suction produced large quantities of blood-stained froth, and considerable inflation with pure oxygen was necessary to secure a return to normal colour. The operation was abandoned. With treatment her condition improved, but about two hours after the commencement of the operation she again became cyanosed. Her pulse was weak and extremely rapid, and large quantities of blood-stained froth were sucked out of the bronchial tree. Half an hour later life was pronounced extinct.

At is was thought that this woman had not fully recovered from the effects of the anæsthetic, her death was reported to the coroner. Post-mortem examination showed the presence of gross pulmonary œdema, moderate hypertrophy of the left ventricle of the heart, and a tumour in the left adrenal gland, which appeared on naked eye examination to be a pheochromocytoma. Microscopic examination confirmed this. The tumour was 1·5 inches in diameter.

Adenomata of the adrenal gland are a comparatively common incidental finding in routine autopsies. They may be confused with small pheochromocytomata, and what appears to be an adenoma may on microscopic investigation prove to be a pheochromocytoma. The true nature of this tumour may be overlooked.

Conclusion.

In retrospect, one can recall cases of sudden or unexpected death in which no satisfactory cause of death was established. In these cases the adrenals were not examined as carefully as they could have been; the real cause of death may have been missed there.

Reference.

GONZALES, T. A., *et alii* (1954), "Legal Medicine", 2nd Edition, page 145.

Reports of Cases.

ADDISON'S DISEASE: REPORT OF A CASE WITH MEDICO-LEGAL INTEREST.

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Coroner's Department, Melbourne.

A MALE Italian labourer, aged forty-seven years, was admitted to hospital on January 26, 1956. Both the patient and his relatives spoke English poorly, the relatives being worried and suspicious about the patient's condition. The history finally obtained was as follows:

For three months he had suffered from a severe burning pain in the upper part of the abdomen; usually coming on one hour after his meals and associated with nausea, frequent vomiting and a sour taste in his mouth. Charcoal powders gave him some relief from the pain without affecting the nausea. He had no appetite during this period and lost one and a half stones in weight. For three weeks before his admission to hospital he had noticed continuous severe back pain with some radiation to the left side. During this three weeks he found that he had an abnormally low morning temperature and heavy sweats during the night. At an out-patient attendance on January 13 his temperature was recorded as 100·2° F. He had had a gastro-enterostomy performed for duodenal ulcer twenty years previously.

Physical examination showed the patient to be a swarthy, stockily built, dark-skinned Italian with spasms of back pain. His temperature was 98·4° F. (this subsequently rose to 99·6° and 100° F. on several occasions), his pulse rate was 100 per minute and his respirations numbered 20 per minute. His blood pressure was 100 millimetres of mercury, systolic, and 80 millimetres, diastolic. The upper part of his abdomen was generally tender, and guarding was present on the left side. An X-ray examination of the patient's chest and excretion pyelography gave results within normal limits, while his hæmoglobin value was 14·2 grammes *per centum*.

A provisional diagnosis of penetrating duodenal ulcer was made, and it was arranged that a barium meal X-ray examination should be carried out some days later. An attempt was made to feed him by an indwelling gastric drip tube, but this had to be abandoned on January 30 because the patient could not tolerate the tube. During this time the patient was very miserable and complained continually of severe back pain. A number 2 hæmatemesis diet was persistently vomited by the patient, and on February 2 he became noisy and disorientated, requiring sedation that night. He was found dead in bed early on the morning of February 3. At no stage during his period in hospital was his blood pressure above 100 millimetres of mercury, systolic, and 80 millimetres, diastolic. On each of several days during his period of hospitalization he had four bowel actions.

The case was reported to the coroner because of the evident distrust of the relatives and the unexpectedness of his death.

At the post-mortem examination the patient was found to be a short, swarthy, middle-aged man with deeply pigmented moles and nipples. Bluish-black pigmentation was present on the buccal aspect of his cheeks and also on the upper jaw. An old left upper abdominal scar was present. The body smelt strongly of paraldehyde. The heart weighed 360 grammes and was flabby but otherwise normal, the coronary arteries being patent and relatively free from atheroma. Examination of the right lung revealed an old calcified Ghon's focus on its lateral surface. A functioning gastro-enterostomy was present, but there was no ulceration anywhere in the gastro-intestinal tract. Both adrenal glands were replaced by firm, yellowish tissue; macroscopic examination revealed no normal adrenal tissue. No other significant features were found on macroscopic examination.

Histological examination of sections of the adrenal glands revealed complete absence of normal adrenal tissue in the four sections cut. Most of the material in the sections was caseous, few giant cell systems being seen. The diagnosis was Addison's disease due to tuberculosis of the adrenal glands.

Discussion.

In forensic medical practice it is common to find that one is dealing with natural disease, a fact which is not sufficiently emphasized in some text-books of forensic medicine and, indeed, hardly mentioned in others.

In this case the patient's death was sudden and unexpected, and no satisfactory diagnosis had been made, while the relatives were considerably disturbed and suspicious.

It is obvious that unrecognized Addison's disease must be considered in any case of sudden unexpected death. There were undoubtedly diagnostic difficulties in this case, because the patient gave a fairly typical ulcer history with a gastro-enterostomy to add emphasis. The language barrier was also a source of difficulty. However, the patient's fever, night sweats and pigmentation inside his mouth were difficult to explain solely on an ulcer basis.

Atrophy of the adrenal glands is now apparently the most common ætiological factor in Addison's disease (Bowden, 1956), but tuberculosis as a cause must still be remembered. Apart from his old quiescent lung lesion, this patient at autopsy showed no evidence of tuberculous infection.

Finally, constant back and shoulder pain is not mentioned in many descriptions of Addison's disease, but should be remembered as a prominent symptom in the tuberculosis-caused Addison's disease.

Reference.

BOWDEN, K. M. (1956), "Some Findings in the Adrenal Glands in Unexplained or Unexpected Death", M. J. AUSTRALIA, 2: 220.

REPORT OF A CASE OF THALLIUM POISONING TREATED WITH THIOURACIL.

By B. L. BEDVILLE AND G. S. SPRAGG,
Royal South Sydney Hospital, Zetland.

FOLLOWING the correspondence of Robert J. Bartholomew in THE MEDICAL JOURNAL OF AUSTRALIA of February 20, 1954, concerning the experimental use of thiouracil against thallium poisoning in rats, we have now to report a case in which this treatment has been used at the Royal South Sydney Hospital on a human subject.

Clinical Record.

The patient, a girl, aged twelve years, and weighing approximately 12 stone, was admitted to hospital at midday on October 13, 1954, having consumed two ounces of "Thalrat" containing 21·8 grains of thallium sulphate the day before. Her first symptoms had appeared on the previous night, when she noticed numbness of the fingers and toes and weakness of the lower extremities. During the morning of the day of her admission to hospital she experienced pain which began in both knees and radiated down the medial aspects of both legs and to the calves. There was no abdominal pain, no nausea and no vomiting.

On her admission to hospital her gait suggested a paresis and possible paræsthesia of both lower limbs, with incipient foot drop. Her mental condition was difficult to assess at that time. She could give a good account of herself, but there appeared to be some psychological disturbance, and we believe that her present mental condition is well above that on her admission to hospital. Our impression is that any mental abberration there was on her admission to hospital was functional rather than toxic.

Examination of the central nervous system revealed the following positive findings: weakness of the dorsiflexors of ankles and toes, hyperæsthesia of the stocking type reaching from the feet to the level of the knees, diminished muscular tone in the feet and ankles and equivocal diminution of the ankle and knee jerks. There were no other abnormal findings in this or any system. The patient's blood pressure was 125 millimetres of mercury, systolic, and 85 millimetres, diastolic. Relevant negative findings were as follows: normal plantar responses on both sides, absence of motor, sensory, cerebellar and proprioceptive disturbance in the upper limbs, absence of cerebellar and proprioceptive disturbance in the lower limbs, and absence of abdominal tenderness.

Immediate drug therapy was instituted. This consisted of the administration of 250 milligrammes of thiouracil every two hours for three days, followed by 600 milligrammes daily in divided doses, together with 20 grains of sodium iodide every six hours. Both drugs were administered orally. Two days later (October 16) the patient began to vomit, and this continued for two days until the sodium iodide therapy was suspended. Thereafter no more of this drug was administered, and the vomiting ceased for the time being. The thiouracil dosage was reduced to 300 milligrammes daily on November 15, to 200 milligrammes daily on November 18, and to 150 milligrammes daily on November 20, and administration was suspended in January, 1955 (unfortunately no record of the exact date can be found).

The peripheral neuritis increased rapidly over the first three days after the patient's admission to hospital, with loss of ankle jerks on the third day. On the sixth day after her admission to hospital the pain and hyperæsthesia in the limbs had decreased and epilation commenced. The following day there was no pain in the limbs, but paræsthesia and hyperæsthesia persisted. Thereafter these symptoms gradually diminished, but muscular tenderness increased and her mental condition began to deteriorate. In addition there was stubborn constipation, giving way on the eleventh day to bouts of diarrhœa with the passage, intact, of the thiouracil tablets. Her appetite had steadily waned during this period. On the fifteenth day after her admission to hospital there was noticeable enlargement of the thyroid gland without signs of glandular dysfunction. The administration of thyroid (British Pharmacopœia), a quarter of a grain twice a day, was commenced on this day. This was reduced to once a day on November 1, and once every two days on November 20, and the treatment was suspended in mid-February.

Her mental condition now showed gross deterioration. She became torpid, stared at the ceiling, uttered animal cries and rarely said anything intelligible. She was incontinent of fæces and urine, vomited frequently and was difficult to feed. Intravenous therapy was instituted. At times, when her mental condition appeared to improve, she uttered loud screams, and acute tenderness in the calves and feet became evident.

On December 3 (fifty days after her admission to hospital) her mental condition began to improve, though incontinence remained. As she continued to improve she became more unmanageable and more noisy. By mid-December it was evident that she was aware of her surroundings and that most of her outbursts were voluntary. Her legs and feet were acutely tender, and she resisted vigorously all attempts to counter the contractures which were developing. By late December she presented a major nursing problem, and as she was causing acute distress to the other patients in the ward and adding greatly to the burdens of an already harassed nursing staff, it seemed inevitable that she would have to be transferred to a mental hospital. When threatened with this, she showed temporary improvement in her attitude. Later she was promised two days at home at Christmas time if she behaved. Her behaviour again improved, but was far from perfect. Nevertheless she was allowed home. On her return to hospital she appeared to have improved, but soon regressed again, and continued to present a problem, though with gradual improvement until January 10, when

her personality showed a sudden reversal. She ceased to complain, smiled and talked happily and was cooperative. About this time regrowth of her hair began. From here on the only problems were the contractures of the knee joints and the gross foot and slight wrist drop. These were corrected under anæsthesia and position was maintained with plaster of Paris splints. Thereafter the patient made gradual improvement. On her discharge from hospital in October, 1955, there remained only bilateral extensor paresis, and she was walking with short leg calipers and extension springs.

Discussion.

It will be appreciated that no conclusions can be drawn from this isolated case as to the place of thiouracil in the treatment of thallium poisoning, but it is hoped that reports of cases in which high doses of the metal have been ingested, and in which the patient has been treated along different lines, may lead to valuable comparative inferences.

Summary.

A case of acute poisoning from a lethal dose of thallium is reported. Thiouracil was used from the outset, and apart from extensor paresis of the lower extremities, recovery was achieved.

Acknowledgements.

We wish to thank Dr. Justin Markell, Dr. Warren Murphy and Dr. Z. Freeman for their encouragement and advice, and Dr. N. J. Royle for his supervision of the orthopædic aspect of the rehabilitation phase. We pay tribute to the late Matron M. Kelly and her nursing staff for their patience and perseverance throughout the patient's illness. Finally, we would again point out that the idea of thiouracil therapy in thallium poisoning was conceived, as far as we know, by Robert J. Bartholomew, whose suggested dosage for the human subject we have faithfully employed.

Reviews.

The Psychiatric Interview, by Harry Stack Sullivan, M.D. Edited by Helen Swick Perry and Mary Ladd Gawel, with an introduction by Otto Allen Will, M.D.; 1955. London: Tavistock Publications, Limited. 8″ × 5¼″, pp. 269. Price: 28s.

This small book's appeal is wider than its title. Its simple language illuminates any doctor-patient relationship, especially if it evokes reflection upon experience and discussion with psychotherapists.

Within the broad biological viewpoint, it reveals special aspects of stimulus-response, the adaptation of organism to environment. This modern psychiatric viewpoint challenges preoccupation with somatic machinery and chemistry: disorder in somatic substrate may be no more necessary for schizophrenia than for the wryness of a smile. Enlightening diagnostic formulation is provided, not by the shifting, ephemeral kaleidoscope of symptoms, but by significant patterns of interpersonal communication, expressive of early acquired maladjustment. Scientific method is focused upon the art of interviewing.

Sullivan, beginning with schizophrenic and obsessive patients, quickly recognized these afflictions as expressive of early acquired maladjustment in social functions, not hereditary weakness or somatic disease. He studied their particular modes of communication and the barriers they tended to erect. This study of interpersonal communication and barrier culminated in his participation in the UNESCO "International Tensions" project.

In "Psychiatry studies interpersonal relations . . ." is truth, but not the whole truth, which may mislead the uninitiated. For the physician and surgeon, clinical phenomena are illuminated by the formulations of anatomy, physiology and psychopathology. The psychiatrist not guided by the formulations of psychology and psychopathology is unguided and misguided. Also, interpersonal relations form but part of the wider field of object relations, embracing inanimate objects, ourselves, moralities, ethics and philosophies, time and space, institutions and numerous quasi-concrete abstractions, such as "the common weal", to which we relate ourselves.

Perhaps the author focuses too sharply upon "effective" exchanges and definite interview-concluding prescriptions to expedite psychotherapy, justifying this with psychoanalysts-of-straw. This may express undue impatience to achieve a limited and preconceived goal: trains of patients with eased but unresolved problems may result. On page 66, "If the interviewer then chooses to violate the confidential relationship . . ." reminds us that neglect of human values is almost the rule for the parents who have founded and fostered our patient's maladjustments. We must earn complete trust.

We learn our skills, from books, by practice and the guidance of more experienced colleagues. Here is much to contemplate, discuss and apply.

Androgens: Biochemistry, Physiology, and Clinical Significance, by Ralph I. Dorfman, Ph.D., and Reginald A. Shipley, M.D.; 1956. New York: John Wiley and Sons, Incorporated. London: Chapman and Hall, Limited. Price: $13.50.

The monograph by R. I. Dorfman and R. A. Shipley on androgens is a monumental work. Every paper which has appeared during the past thirty years on the subject of androgens and related substances seems to have been considered. For example, in the chapter on actions of androgens on sex structure of animals there are 208 references.

The first section of the book, 139 pages, deals very fully with the biochemistry of androgens and related steroids with very detailed organic chemistry. The names and structural formulæ of the compounds are collected together in an appendix which occupies 73 pages. The section on the physiology of the androgens, which occupies 104 pages, deals with the actions of the androgens on sex structures in man and animals, on other endocrine bodies, on metabolism and enzymes and on behaviour. The last section of 318 pages deals very extensively with clinical aspects.

Finally there are four appendices, one already mentioned, one on the preparation of urinary extracts for 17-ketosteroid and androgen assay, one on androgen bioassay methods, and one on chemical assay methods.

No details which could have any scientific or clinical interest seem to have been omitted. Medical readers would find the biochemistry and structural chemistry extremely hard going, but at least one does not have to refer to another book for any details. The clinical section is very detailed, androgen therapy and the excretion of androgens and 17-ketosteroids are dealt with very fully.

The book is a mine of information about androgens and will be an invaluable reference book on all aspects of the subject. The reported efficacy of androgens in a variety of conditions has been considered critically.

Fundamentals of Internal Medicine, by Wallace Mason Yater, A.B., M.D., M.S. (in Med.), F.A.C.P., with the assistance of William Francis Oliver, B.S., M.D., A.A.C.P.; Fourth Edition; 1954. New York: Appleton-Century-Crofts, Incorporated. 10″ × 7″, pp. 1306, with about 150 illustrations. Price: $13.50.

The fourth edition of Yater's "Fundamentals of Internal Medicine" follows the pattern of previous editions and remains quite a good and useful synopsis of medicine. That this is the purpose of the book is revealed in the preface, where the author answers the criticism that the material is too brief by stating his purpose as being "to relieve as much as possible the overburdened student or practitioner who really needs a book that will save him reading time". The format with the main headings picked out in heavier type and often a summary at the end of a section assists in this direction. The summary is frequently, however, unsatisfying on account of its brevity.

As a text-book from which a student should learn his medicine, the book seems inadequate, being too much a collection of isolated facts and dealing too little with the principles underlying them which give them meaning. It may be useful for revision or for "cramming" for examinations.

It may have more appeal to the practitioner, especially the practical chapters at the end on dietetics, antibiotics and chemotherapy, inhalational therapy *et cetera*, which, though brief, are well done.

The edition has been thoroughly revised. A most useful section on ACTH and cortisone is included, but the classification of diseases according to their response to the drugs seems rather

involved and confusing. On the whole the information is up to date, although one is surprised that the intrathecal use of streptomycin is still advised in the treatment of tuberculous meningitis. It would seem, too, that the chemotherapy of pulmonary tuberculosis has not been given the prominence which is its due, being described as "far from adequate", but a "valuable adjunct". It is surely more useful and important than collapse therapy. The thoroughness of the revision is indicated by the fact that several misleading statements criticized in the review of the last edition have been corrected.

The book is well produced and freely illustrated. The illustrations are of a high standard and reproductions of radiographs are of good quality. Although containing a mass of useful material, one feels that the book cannot be recommended to replace those at present in vogue in the medical schools of this country.

The Sequelæ of Amputation, by Keith C. Bradley, F.R.A.C.S.; 1955. Published by the Trustees of the Services Canteens Trust Fund (Australia). 8¼" × 5¼", pp. 243. Price: 10s.

AFTER the war the trustees of the Services Canteen Trust Fund sponsored a comprehensive investigation and research into the disabilities of amputees. Mr. Bradley was selected for the task, and a three-year programme was outlined—the first two in the Melbourne Medical School under the guidance of Professor Sunderland, and the third year in a visit overseas to Britain, Europe and North America to study what steps were being taken there. On his return Mr. Bradley outlined the results of his work in the present book.

In the earlier chapters the anatomical and pathological changes in amputation stumps are fully described, and also the surgical and other procedures which are used. Full clinical histories are given of a large number of patients, and the results of treatment are discussed. Particular attention is given to the distressing problems of painful stumps and "phantom limb". Nerve blocking, excision of neuromata, percussion ultrasonic therapy, rhizotomy, cordotomy, sympathectomy, cortical resection and prefrontal leucotomy are fully discussed, and the results recorded. The literature, both British and foreign, is fully reviewed.

The author also outlines the set-up in other countries for dealing with amputees, particularly in England, where it is evident that more effective arrangements are available than those in Australia, particularly for civilian amputees.

Amongst other recommendations, the author advises:

1. A greater appreciation by the profession of the sequelæ of amputation and the needs of amputees for rehabilitation.

2. Enlargement of limb manufacturing facilities to overcome the present difficulty of obtaining an artificial limb in a reasonable time.

3. Rehabilitation centres for fitting and training in the use of an artificial limb.

4. A government-sponsored programme, providing artificial limbs and rehabilitation services to all amputees, whether ex-servicemen or civilians.

The book can be confidently recommended to all practitioners concerned in the management of these patients, and it is hoped that steps will be taken by service and civilian departments to implement the recommendations.

From Witchcraft to Antisepsis: A Study in Antithesis, by Douglas Guthrie, M.D., F.R.C.S.; Logan Clendening Lectures on the History and Philosophy of Medicine; Fifth Series; 1955. Lawrence: University of Kansas Press. 8¼" × 5¼", pp. 64. Price: $1.50.

IN a neat little volume, the University of Kansas has published two interesting essays written by Dr. Douglas Guthrie, Lecturer in the History of Medicine, University of Edinburgh, and they provided the substance for a Logan Clendening Lecture delivered by him in 1955. The essays, described as a study in antithesis under the intriguing titles "Witches and Witch-Doctors" and "Lister and His Achievement", are faultlessly presented in immaculate prose. However, it would seem that little new ground has been opened up in the selection of material, and that considerable restraint has been exercised in a careful avoidance of controversial issues and apt philosophical comment. Even a modicum of judicious speculation may add spice to the reading of historical commonplaces.

Our confused notions about the occult science of witchcraft probably stem from occasional references in the Hebrew scriptures, which sought to discourage adherence to the Babylonian theories of divination, astrology or demonology as being inimical to the teachings of Moses and the prophets. Since time immemorial ambitious people have tried to invoke the power of a supreme authority for purely selfish reasons; and disappointed suppliants have not hesitated to flout the moral law by seeking the required help of unorthodox supernatural agencies as a short cut towards the attainment of their desires.

The notorious witch of Endor would appear to be the exact prototype of a modern spiritualistic medium endowed with a special gift of being able to recall magically and then to hold converse with shades of the departed before deciding upon a course of action in unison with certain familiar spirits. And so King Saul, finding himself in a predicament, was tempted to consult this unnatural woman, knowing full well that in doing so he was deliberately breaking the Mosaic law as well as his own tribal decree that all such sorcerers were to be sought out and sent into exile. In a desperate situation he merely took the obvious short cut at all cost to obtain the necessary assurance that on the morrow his victory over the Philistine army would be complete.

The mediæval onslaught against witchcraft and the demoniacal interference with innocent victims by inward possession or by outward obsession, was based largely upon the current Christian dogmas, fully assisted by the ignorance, superstition and fear of the masses. And it may be stretching the imagination a little too far to contrast this strange concatenation of religious ideas and the consequential inhuman régime of cruelty and injustice with the beneficent and essentially humane motives of Joseph Lister in seeking truth and perfection by way of the modern scientific method.

Many will find intellectual satisfaction in the reading of these two well-written essays. There is still much to be gained from a fresh study of those vital principles which at the end of last century so radically transformed surgical theory and practice.

Morality Fair: Vagaries of Social Conduct as Reflected in the Press, by Geoffrey Williamson; 1955. London: Watts and Company. 8" × 5", pp. 274, with many illustrations. Price: 15s.

GEOFFREY WILLIAMSON, former editor of *John Bull*, has given in "Morality Fair" a timely reminder of changing viewpoints on moral issues. The book is written as a sociological survey for the average man. The object of arousing interest in present-day sex problems is achieved through a frank discussion of factual evidence largely gleaned from the Press, and illustrated by contrasting photographs. As an example, Manet's nude in "*Le déjeuner sur l'herbe*", which shocked the Victorians, appears on the same page as a modern outdoor nudist, who, though more flagrantly devoid of clothes, would today cause no comment. On another page one views the prim Mrs. Lambert, tennis ace of 1913, and "Georgeous Gussie" of today. Whilst change in outlook is inevitable, the author draws attention to the wide divergence of present public opinion. One homosexual may be punished, whereas another is acclaimed. A classic is banned, a salacious sex magazine is sold with impunity.

The chapter on "Profane Love's Social Impact" deals with the problem of illegitimacy, procuration, abortion and prostitution. There is a plea for a better understanding of causation.

"Sex in the Courts" deals with frequent criticisms of the Press on its over-coverage of sexual crimes. These are countered by factual statements as to the enormous numbers which receive no publicity whatever.

"Birth Control" and automatic machines for selling contraceptives are dealt with under the heading "When Science Intervenes".

A chapter on sex crimes draws attention to staggering increases in numbers, particularly after the last war. Whilst the author cannot offer any easy solution to the thought-compelling problems which are uncovered, he pays tribute to the successes of the great reformers, including Josephine Butler, who founded the Association for Moral and Social Hygiene, Mrs. Seaton-Tiedeman, who created the Divorce Law Reform Union, and Ellice Hopkins, founder of associations for the care of friendless girls.

There is a final comment: "With so many well-meaning people tackling social problems and drawing upon such a wealth

of experience, the augury for the future should be bright. But is it? We have seen the progress made in a hundred years of moral crusading. What will the next century reveal?" That success will depend on widespread understanding of the difficulties is undeniable. "Morality Fair" presents members of every profession with an intriguing approach to the subject.

The Relief of Symptoms, by Walter Modell, M.D., F.A.C.P.; 1955. London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9" × 6¼", pp. 459. Price: £4.

DR. MODELL considers that treatment of specific symptoms should go hand in hand with the treatment of the causal complaint, and advocates the alleviation of distress pending the establishment of a diagnosis. The wisdom of this cannot be denied provided there is no danger or possibility of clouding an accurate diagnosis. He, however, is of the opinion that too little attention is paid to this aspect of therapy, and has written this book on the subject.

"The Relief of Symptoms" is divided into two parts, the first dealing with "Theory" and the second with "Practice".

The use of placebos is considered to be both justifiable and good medicine, and the distinction between pure placebos and the placebo action which may be present in all forms of treatment is discussed.

In the second portion of the book reference is made to the action and dosage of drugs for prophylaxis, relief, and maintenance. In this section pain is given prominence, and the various approaches for its relief are described. Stress is laid on the dangers of addiction, especially with morphine and its derivatives. New drugs are referred to throughout the book, and a timely warning is given on their too ready acceptance. This includes a chapter on cortisone and ACTH. The importance of giving relief without resorting to drugs in insomnia is emphasized.

It could well be that the people having infrequent bowel actions, who the author states are in good health, may not know what it is like to feel well.

Dr. Modell has given us a readable book, with an up to date account of symptomatic treatment. Every respect must be paid to the opinions expressed on the subject by a man who is both a pharmacologist and a practising physician. He states that "The Relief of Symptoms" is not intended to be a heavy text-book, and is primarily for students and young practitioners. Provided the student is able to realize fully the dangers of symptomatic treatment, the reading of this book will provide him with relaxation from studying the standard text-books so necessary for his training.

Antibiotics in Nutrition, by Thomas H. Jukes, Ph.D.; 1955; with a foreword by Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D. New York: Medical Encyclopedia, Incorporated. 9" × 6", pp. 127. Price: $4.00.

IN 1949 a group of workers using chlortetracycline ("Aureomycin") fermentation residues as a source of a growth factor for chickens (now vitamin B_{12}) discovered that the traces of "Aureomycin" left in the mash caused the chickens to which it was fed to grow at a greater rate than the controls. Very many experimental nutritional studies have been made in the last five years on the effect on growth of a variety of animals, including man, of the addition of small amounts of antibiotics, particularly chlortetracycline ("Aureomycin"), oxytetracycline ("Terramycin"), penicillin and streptomycin. Thomas H. Jukes has collected in his book all the available data on the matter.

The extraordinary amount of interest taken in the subject is shown by the fact that the author cites 439 references. After a short introduction on the chemistry of the antibiotics, the author treats in detail the mechanism of antibiotic growth effect in chicks, turkeys, pigs and ruminant animals. The main conclusion is that very small doses of certain antibiotics prevent the growth of microorganisms in the gut which slow down growth of the animal. If the animals are brought up in particularly clean surroundings the antibiotics have little or no effect. There is a section on the effect of feeding antibiotics on the requirement for nutrients. Then follows a discussion on antibiotics in animal production, and finally a section on the physiological effects of dietary antibiotics. The author seems to have tried to introduce material from all of the 439 papers he cites, and that without much critical judgement. There is a great deal of repetition, many contradictory statements are made, and a complete lack of statistical evaluation of the results claimed is shown. The book would be much smaller, more readable and more useful if it were very thoroughly edited. The information is there and no doubt the book will be very useful to anyone who wants to know what has been published on the subject.

The author does not make any extravagant claims for the use of antibiotics in animal feeding; indeed, the first sentence of his concluding section is: "An apparent improvement in the nutritional status of animals may be often produced by adding small quantities of certain antibiotics to the diet."

Obstetrical Roentgenology, by Robert Berman, M.D., F.A.C.S.; 1955. Philadelphia: F. A. Davis Company, Publishers. Sydney: Angus and Robertson, Limited. 9¼" × 7", pp. 614, with 486 illustrations. Price: £6 17s. 6d.

THIS book is written by an obstetrician, who is also a most able radiologist, and it should appeal to all those who are interested in both specialties, because it condenses practically all aspects of the subject into one volume. Up to the present time it has not been possible for an obstetrician, unversed in the principles and practice of radiology, to acquire a practical knowledge of the subject, owing to the number and variety of references scattered throughout the medical literature.

The book is well illustrated, and the numerous radiographs are reproduced in their original negative form. The material which forms its basis was derived from an experience of approximately 2500 obstetrical cases, each of which was studied by X-ray pelvimetry; the clinical results were correlated with the radiological findings in order to develop skill in film interpretation.

The author wisely stresses the fact that the function of X-ray pelvimetry is not to predict the outcome of labour or to prove or disprove whether vaginal delivery is possible; it merely shows the size and variations in shape of the pelvic inlet and bony walls of the pelvic cavity and outlet. It also shows the size, position, attitude and skeletal structure of the fœtus and, possibly, the site of implantation of the placenta. Historical considerations, technical aspects, and especially the clinical aspects of X-ray pelvimetry, are dealt with in separate chapters.

The clinical and radiological classifications of the pelvis are fully discussed and illustrated, but the chapters dealing with the *fœtus in utero* and the localization of the placenta, though comprehensive, seem to be somewhat brief by comparison with the remainder of the book. The cystographic method of localization of a low or pelvic implantation of the placenta receives too much emphasis. All methods of X-ray pelvimetry and cephalometry are fully discussed, and the author suggests that simplicity and standardization of technique are desirable in order to compare results in various medical centres and in other countries.

Although the book contributes nothing new in obstetrical radiology, it is a welcome addition to medical literature in that it correlates the many references which have accumulated since the discovery of X rays, and which have been contributed by obstetricians and radiologists. The bibliography contains 437 references divided into the headings of "Reference Books", "Pelvis", "Fœtus" and "Placenta".

Analgesia for Midwives, by Hilda Roberts, M.R.C.S., F.F.A.R.C.S., D.A., D.C.H.; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 8½" × 5½", pp. 75, with many illustrations. Price: 10s. 6d.

THIS book achieves its object—it is easy to read, the explanations are very clear, and the illustrations well chosen and adequate.

The chapter on ante-natal preparation is nicely placed and well done. Dr. Roberts wisely confines herself to a few well-tried drugs. The description of the apparatus and the use of nitrous oxide and air, and trilene, is excellent, and should leave the midwife quite clear in her mind about the administration and control of these analgesics.

The resuscitation of the newborn is in keeping with the remainder of the book and is very well done. The rocker recommended must be rare in Australian hospitals and in domiciliary practice, and the only other method of artificial respiration mentioned is mouth-to-mouth breathing, which is condemned. Discussion of the various methods of artificial respiration in the newborn would be an advantage.

An informative description of regional anæsthesia should impress the midwife with the necessity of having the requirements correctly prepared and set out. It would be helpful to have a list of the necessary apparatus for each procedure.

This book will appeal to all nurses associated with obstetric practice, especially those in far distant places.

Atlas of General Surgery, by Joseph R. Wilder, M.D.; 1955. St. Louis: The C. V. Mosby Company; Melbourne: W. Ramsay (Surgical), Limited. 13¼" × 10½", pp. 222, with 101 plates. Price: £7 8s. 6d.

IN this book the author deals in turn with most of the common major surgical procedures. He does not deal with more specialized operations—for example, those in the fields of neurosurgery, cardiac and thoracic surgery and orthopædics. In most cases the description of the operation is approached in a standard fashion. A brief introductory statement about the operation is followed by a series of "important considerations"; then the operation is described in stages, each stage being illustrated separately. The illustrations have been skilfully and effectively drawn and form a major contribution to the book. The author states that the techniques described in the book are those which he has found most satisfactory. He makes no claim that they are original, or that there are no other satisfactory methods. However, they are intended to teach sound surgical principles to young surgeons, who can then develop their own personal techniques in detail. This is a handsome and helpful book, but we wonder if many young surgeons will care to pay the price required for its purchase.

Assay Methods of Antibiotics: A Laboratory Manual, by Donald C. Grove, Ph.D., and William A. Randall, Ph.D., with a foreword by Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D.; Antibiotics Monographs No. 2; 1955. New York: Medical Encyclopedia, Incorporated. Distributors: New York and London—Interscience Publishers, Incorporated. 9" × 6", pp. 204, with 42 illustrations. Price: $5.00.

IN the short spell of fifteen years thousands of antibiotic substances have been isolated in the many research laboratories throughout the world. At an early stage in the examination of these substances assays methods have had to be developed, often crude and lacking in precision, but for the seventeen useful antibiotics on the market today this is certainly not now the case. Assay methods for these are well established and of known and calculable accuracy.

This book is the first and only compilation of practical methods of assay for these agents. Many of the methods are those in use by the Federal Food and Drugs Administration, and therefore have "official" status in the United States of America.

The methods described include those for determining the potency of such pharmaceutical preparations as tablets, troches and ointments, as well as those applicable to the pure drug. A chapter is devoted to the differential analysis of mixtures of antibiotics, and two chapters deal with tests for toxicity, pyrogenicity, sterility and histamine content.

The methods are described in a comprehensive and detailed manner, and there should be little difficulty in the competent use of them by the skilled laboratory technician. The ultraviolet and infra-red absorption spectra of the antibiotics are also collected together in this volume, together with a variety of other optical methods of analysis.

In the case of this book the description "monumental" cannot be avoided, not for its size, but for its place in this field of analysis and for the task so very ably accomplished by the authors. It is certainly an essential in any laboratory where antibiotics play even the most minor role.

The Year Book of Medicine (1955–1956 Year Book Series), edited by Paul B. Beeson, M.D., Carl Muschenheim, M.D., William B. Castle, M.D., Tinsley R. Harrison, M.D., Franz J. Ingelfinger, M.D., and Philip K. Bondy, M.D.; 1955. Chicago: The Year Book Publishers, Incorporated. 8" × 5", pp. 712, with 121 illustrations. Price: $6.00.

A LARGE amount of material in abstract form has been packed into this volume by the same six authors as prepared its predecessor. In Part I, Paul Beeson arranges his material under the headings of immunity and infection, studies of antibiotic action, untoward effects of antibiotics, staphylococcal and streptococcal infection, erysipeloid, salmonellosis, brucellosis, cholera, pasteurollosis, non-specific bacterial infections of the lungs, tetanus, leprosy, fungous diseases, amœbiasis, measles, rubella, rabies, mumps orchitis, infectious mononucleosis, other virus diseases, new (?) diseases, arthritis, helminthiasis, rheumatic fever, systemic *lupus erythematosus*, chronic inflammatory syndromes of uncertain ætiology, fever and miscellaneous subjects. Carl Muschenheim deals with the chest in Part II. He has chapters on physiology, emphysema, bronchitis, asthma, congenital disorders, neoplasms, pneumonokoniosis, pulmonary mycoses, sarcoidosis, tuberculosis and miscellaneous subjects. Part III, that on the blood and blood-forming organs, is edited by William B. Castle, who deals in turn with general considerations and special techniques, hæmolytic anæmias, pernicious and other nutritional macrocytic anæmias, hypochromic anæmia, other anæmias, polycythæmia, leucopenic states, leuchæmia and related disorders, vascular and thrombocytopenic purpuras and coagulation defects. Part IV, on the heart and blood vessels and the kidney, edited by Tinsley R. Harrison, has chapters on congenital heart disease, valvular disease and murmurs, hypertension, coronary disease, congestive failure, electrocardiography and arrhythmias, cerebral vascular disorders, peripheral vascular disease and the kidney. In Part V, which deals with the digestive system, Franz J. Ingelfinger has arranged his material in three chapters, which cover respectively the stomach and duodenum, the intestines, and the liver, gall-bladder and pancreas. The subject of the sixth and last part is metabolism. Here the editor, Philip K. Bondy, has prepared chapters on the thyroid gland, the adrenal glands, the pituitary gland, carbohydrate metabolism, calcium, phosphorus and the parathyroid glands, nutrition and body composition, and metabolic diseases. This Year Book is very comprehensive in its scope, and there are few, if any, practising doctors who will not find in it valuable material from the current medical literature.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Urology", by B. G. Clarke, M.S., M.D., F.A.C.S., and Louis R. M. Del Guercio, M.D.; 1956. New York, Toronto and London: The Blakiston Division of the McGraw-Hill Book Company, Incorporated. 9" × 6", pp. 255, with many illustrations. Price: $6.50.

The authors have tried to provide "a short essential text brief enough to be read during an undergraduate course in urology or used for review", with diagrams, reproduction of X-ray films, photomicrographs and references.

"Biochemistry of the Eye", by Antoinette Pirie, M.A., Ph.D., and Ruth Van Heyningen, M.A., D.Phil.; 1956. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 330, with illustrations. Price: 35s.

The authors have written this book for three reasons: (*a*) although the eye is part of the body, it is so significant that any biochemist who works with it elevates it to a special place; (*b*) few biochemists at present work with the eye; (*c*) the clinical study of ophthalmology can be more interesting and fruitful if the biochemistry of the eye is understood.

"Clinical Psychology: The Study of Persons", by Richard W. Wallen, Ph.D.; 1956. New York, Toronto and London: McGraw-Hill Book Company, Incorporated. 9" × 6½", pp. 401. Price: $6.00.

The author has tried to write the book "around the idea that the first clinical course should aid students to think creatively about the many kinds of data obtained in studying persons".

"A Synopsis of Contemporary Psychiatry", by George A. Ulett, B.A., M.S., Ph.D., M.D., and D. Wells Goodrich, M.D.; 1956. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical), Limited. 7½" × 5", pp. 243. Price: £2 17s. 9d.

Intended as a quick reference "for psychiatric residents, medical and psychological interns, medical students, nurses and others who work in the psychiatric clinic and hospital".

"Obstetrical Practice", by Harold Speert, M.D., and Alan F. Guttmacher, M.D.; 1956. New York: Landsberger Medical Books, Incorporated. 8" × 5½", pp. 478. Price: $7.00.

Intended for the general practitioner.

The Medical Journal of Australia

SATURDAY, AUGUST 11, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE WORLD POPULATION PROBLEM.

THE problem faced by humanity because of the ever-increasing population of the world has been referred to recently in medical and non-medical journals. It has been brought to the attention of this journal by receipt of a book entitled "Adaptive Human Fertility" by Paul S. Henshaw, Ph.D.[1] This is a well constructed and thought-provoking volume and should be read by everyone who gives serious thought to the problem. The author, in his preface, describes himself as a biologist, or "perhaps it would be permissible to say" a human ecologist. He began this work during the thirties when he was at the Marine Biological Laboratory, Massachusetts, and after carrying out some work in Japan at the end of the second World War, he joined the Division of International Health of the United States Health Service. He is thus in a position to know something about his subject. In his introduction he states that the purpose of the book is to deal with the problems of fertility and also the question: "Is the increase in number of people too rapid, and, if so, what sensible steps can be taken?" Our intention is to deal with some of the main points in his argument and to mention views which have been expressed in other publications.

To begin with, the population of the world, we are told, is approximately 2·5 billion people and the annual rate of increase is about 1·2%. In other words there appear on earth each year more than 30,000,000 additional mouths to be fed—more than 80,000 a day. "Never before have there been so many people on the earth; never before has the number been increasing so rapidly; never before have demands for resources been so great." There are three types of thinkers in regard to the question whether the earth will be able to provide for its people. In the first place the optimists insist that the bounties of the earth are almost limitless; secondly, those who are indifferent trust that somehow or other Providence will provide; the third group are the realists who take into account the meaning of population growth for what it is, both with respect to food and resources and apart from them. Obviously it is preferable to belong to the third of these groups. In these circumstances we must ask what the carrying capacity of the earth is when all existing land and resources are being utilized to the maximum and with the greatest efficiency. It does not need a wise man to point out that all available resources are not being exploited to the full and also that there are possibly resources of which we have no knowledge. A fantastic opinion by Harrison Brown is quoted: "If we were willing to be crowded together closely enough, to eat foods which would bear little resemblance to the foods we eat today, and to be deprived of simple but satisfying luxuries such as fireplaces, gardens, and lawns, a world population of 50 billion persons would not be out of the question. And if we really put our minds to the problem we could construct floating islands where people might live and where algæ farms could function, and perhaps 100 billion persons could be provided for." Henshaw adds that one hundred billion will be reached in less than 500 years at present rates of population growth. Henshaw, on the evidence offered, cannot see that population growth at present rates will continue for long. He therefore wants to know whether the rates will be reduced by the spread of poverty and want, by intelligent fertility management or by some other means. We have always been told that three factors operated to keep the world population from becoming excessive—famine, pestilence and war. Though in many countries the Calorie requirements of the people are not being met as they should be, the world is sufficiently realistic not to allow famine on a large scale to make great inroads on the population. Again, medical progress has advanced at such a rate that pestilence is not likely to exact a heavy toll on the people of any country; and war of the standard of the second World War will not halt the growth of population for more than a matter of some months. In regard to "intelligent fertility management" we come on to debatable ground. Henshaw has a chapter which he entitles "Inherent Conflicts". In the first place, discussing interference with Nature, he deals with Nature's wastage of life and the views held by "religious groups". We need not deal at length with this aspect except to state that objections to fertility control, held on ethical or religious grounds, must be treated with respect. Henshaw concludes this part of his discussion with an obvious statement: "Whether conception control is contrary to divine plan, and whether the prevention of conception or the prevention of birth constitutes what must be defined as the wilful taking of life, are matters on which views are not uniform." Under the heading of "Moral Values" he makes a plea for increased knowledge and understanding of sexual matters generally. There is danger, not from the availability of knowledge, but from its incorrect use. In this chapter Henshaw deals with

[1] "Adaptive Human Fertility", by Paul S. Henshaw, Ph.D.; 1955. New York, Toronto, London: The Blakiston Division, McGraw-Hill Book Company, Incorporated. 9" × 6", pp. 336, with 28 illustrations. Price: $5.50.

regional philosophies—a question which has the greatest possible bearing on the adoption of fertility control measures by some of the nations whose populations are at present most overcrowded. He points out that the regard for life is different as between the United States and Western Europe on the one hand and the Far East on the other. The Orient, as shown in the recent Korean war, showed a willingness to sacrifice the lives of poorly trained troops, and this willingness "does in some measure go hand in hand with availability of human beings". Henshaw suggests that the fatalism of the Orient—the suppression of ego-centred desires and a demonstration of ability to endure—represents adaptation to overcrowding. "Where fatalism and overcrowding go hand in hand and where the endurance of hardship is regarded as a virtue, the acceptance of fertility guidance, if it is accepted at all, is likely to be for different reasons." Henshaw discusses whether we can really attribute the fatalism of the East to overcrowding and spreading poverty. We need not concern ourselves with this, or with other phases of this part of the subject which do not deal with its broad aspect. The "plan of management" put forward by Henshaw is one of "adaptive fertility" or teleogenesis. By this he means a planned life or planned beginning of life, and implies through the feature of planning, "option based on judgment by those in a position to grant the privilege of life". Confidence that the plan is workable is based on two assumptions: (*a*) that completely acceptable methods of fertility control will be developed, and (*b*) that there is a general desire of people everywhere to keep family size in balance with means of support. Two "simple principles" are involved—voluntary parenthood and responsible parenthood. Henshaw stages an interesting and earnest discussion on his ideas, but in answer to his opening question about the rapid increase in the number of people and what "sensible steps" can be taken, we must hold that his whole scheme is unpractical. One cannot imagine that the millions of people in India, China and Indonesia, to name only three countries, could ever be brought to think seriously about voluntary parenthood and adopt it.

An up-to-the-minute review of the problem comes from Sir Solly Zuckerman, F.R.S., of the University of Birmingham.[1] The title of this article is "Physiological Control of Population Growth"; it is concerned mainly with the report of a conference held at Tokyo at which the subject was discussed by economists, social workers, and students of reproductive physiology. This conference came about in an interesting way. After some preliminary discussions between the Planned Parenthood Federation and the Committee on Reproduction of the National Research Council, the National Academy of Sciences in 1952 convened a meeting out of which emerged a new organization called the Population Council. Dr. Warren O. Nelson, professor of anatomy of the State University of Iowa, was appointed medical director of the Council. This council assisted the International Planned Parenthood Federation to call the Tokyo meeting. Zuckerman explains that rates of reproduction are high, not because of any increase in fertility, but because of sharp declines in mortality rates brought about by such events as the elimination of malaria subsequent to the discovery of DDT. In Japan the situation, at the time of the conference, had become so serious that abortion had been legalized in an effort to reduce the strain of increasing numbers on the national economy. Work was reported on the use of steroid hormones and plant extracts which had been used in an attempt to interfere with the action of gonadotrophic hormone, and mention was made of investigations into the part played in mammalian fertilization by hyaluronidase and hyaluronidase-inhibitors. In addition reference was made to new work on anti-gonadotrophins. In every instance the results were looked on as ineffectual, doubtful or unsuitable. Zuckerman has in mind the application of the methods under discussion to the Asiatic world, because he refers to one of the promising procedures as not likely to have any general application in the greater part of this area. J. B. Thiersch told a "dramatic story" of the abortifacient action of certain metabolites. Some of the preparations studied failed to destroy rat fœtuses, and when this happened the young usually developed abnormally and were born in a malformed state. One preparation was given a clinical trial on 26 patients in whom pregnancy had to be terminated for medical reasons. In most instances the drug acted as an effective abortifacient; in the remainder there were complications and then the fœtus was abnormal or general ill-effects occurred in the mother. Zuckerman writes: "It was clear from this, as from all other physiological papers of the conference, that the practical goal of all these urgently needed researches—the discovery of a 'pil' which can be taken by mouth, and the only physiological effect of which would be that of inhibiting the development of the fertilized ovum, or of suppressing ovulation or gametogenesis at will—is so remote from realization that at this stage no one can say how, when or even whether success will ever be achieved." This means that no answer can be given to the question posed by Henshaw, about the taking of "sensible steps" in regard to the increase of population.

One point remains. Zuckerman adds after the words just quoted that much study would have to be carried out in the field before it would be possible to say how different peoples would react to efforts, sponsored or not, to spread a knowledge of birth control. The pressure of population on resources is being felt most acutely in areas which have never known anything but illiteracy, poverty, overcrowding and squalor. Western methods of birth control cannot be used in such conditions. Zuckerman thinks that the situation would be transformed if the "pil" of which he writes was ever discovered, but insists that it would have to be 100% certain. This makes us recall what Henshaw referred to when he discussed his "regional philosophies". *The Lancet* in an editorial in the issue of January 21, 1956, puts the matter with admirable bluntness. It is stated that any suggestion that the West was trying to produce a substance with which foodstuffs could be doctored and the fertility of Eastern peoples reduced "might release a reaction far more powerful than the Indian Mutiny precipitated by the use of pig grease on cartridges". It adds that such suspicions have been voiced. The only positive idea that emerges from this whole discussion is expressed by Zuckerman, who writes that the West will be doing nothing but good if it continues to press on with the kind of physiological research of which the Tokyo meeting provided so useful a résumé.

[1] *Nature*, January 14, 1956.

Current Comment.

THE EPIDEMIOLOGY OF ACUTE MYOCARDIAL INFARCTION.

VARIOUS IMPRESSIONS on the relative incidence of the acute myocardial infections have gained considerable ground with the increased awareness of the extraneous factors in the causation of atherosclerosis. From time to time, suggestions are made that the incidence of myocardial infarction is increasing throughout the general population. It is also suggested that myocardial infarction is indirectly related to sex, race, general activity, and metabolic abnormalities such as *diabetes mellitus*. The statistics relating to the incidence of myocardial infarction are not only interesting, but they also acquire a particular importance if the arterial disease is found to be preventible. Figures are available which make comparison of any changes in incidence detectable. K. T. Lee and W. A. Thomas[1] have made a survey based on all the post-mortem examinations carried out at the University of Washington from 1910 to 1954. In all, over 8000 autopsies were performed upon adult subjects, and the principal diagnosis in 500 cases was one of myocardial infarction. Of the subjects in whom death was due to myocardial infarction, 66·8% were men whose average age was sixty-one years, while that of the women was sixty-four years. Of the subjects in whom infarction was present, 19·6% had been diabetic subjects, the incidence being particularly high in women. The general incidence of *diabetes mellitus* in the series was 5·1%, so that the incidence of diabetes in cases of myocardial infarction was significantly raised above this figure. In all age groups the finding of myocardial infarction at the autopsy examination increased through the years. In the 1910 to 1919 decade the incidence was 0·5% and in the 1945 to 1954 decade it was 10·2%. The relative incidence of myocardial infarction in live patients throughout the later years of the survey followed the same trends as the figures obtained in the examination of those who died. However, it was noted that the average age at death in all cases had risen throughout the years of the records from forty-eight years for men and forty-two years for women in the first decade, to fifty-seven years for men and fifty-three years for women in the final decade. This tends to indicate either that more older people were admitted to the hospital in later years, or that the survival age was raised with the increased likelihood of myocardial infarction. In fact, Lee and Thomas found that there was an increased incidence of myocardial infarction at all ages, which rather obviates the influence of increased longevity. The influence of accuracy in diagnosis at the different periods was not considered to be of particular importance. The influence of geographical factors is difficult to ascertain, though early figures given for autopsy series in both Japan and Massachusetts agree quite well with the incidence at that time in this Washington series. Particularly striking is the finding that there is a twenty-fold increase in the incidence of death by myocardial infarction between the first and the last decade of the survey. The influence of *diabetes mellitus* appears to be considerable, being four times in women with infarction and three times in men with infarction as common as in the general autopsy series. This agrees roughly with the findings of B. J. Clawson and E. T. Bell,[2] who suggested that diabetes accelerates atherosclerosis of the coronary arteries, particularly in females. Clawson and Bell suggested that diabetes was almost sufficient to bring the incidence of myocardial infarction in affected females up to the same level as in affected men. This difference in sex ratio of non-diabetic patients with infarction has for long been accepted. R. F. Ackerman, T. J. Dry and J. E. Edwards[3] found that in a large series of post-mortem examinations on female subjects, the incidence of atherosclerosis rose from 5% in the fourth decade of life to 60% in the eighth decade. The incidence was less in the undernourished women and greater in the diabetics, though not so apparently marked in the latter cases than in the series of Clawson and Bell and of Lee and Thomas. When the findings in the autopsies on females of Ackerman *et alii* were compared with a similar series carried out on men by M. K. White, J. E. Edwards and T. J. Dry,[1] it appeared that the incidence of severe atherosclerosis was considerably higher in middle-aged men than in middle-aged women. In the men, the atherosclerosis increased rapidly from the thirty-year age group, reaching a maximum in the sixth decade of life and thereafter remaining at a steady level. On the other hand the incidence of atherosclerosis in women continued to rise and to approach the male incidence in later life. However, it is to be noted that in the more recent autopsy series of Lee and Thomas, the male to female sex ratio of death by myocardial infarction in the last decade was 1·1:1, which indicates that the influence of sex is not of great importance. That this relative sex equality is a recent trend is shown by the finding of a 2:1 sex ratio in the Washington autopsy series prior to 1940. From the whole series it was evident that the age of women who died of myocardial infarction was greater than that of the men. This indicates that the female hormones, while delaying atherosclerotic changes, have little effect on the ultimate outcome.

W. B. Wartman and H. K. Hellerstein[3] had found a general incidence of 8·2% of myocardial infarction in a large autopsy series, and they suggested that in 25% of the whole series there was significant disease of the coronary arteries. They also found that single infarcts were more common in men and multiple infarcts were more common in women. J. A. Ryle and W. T. Russell[3] made some pertinent suggestions on the prevention of atherosclerosis and coronary disease in predisposed groups in the community. They reported that in England and Wales the mortality from coronary disease increased 15 times between 1921 and 1945, and, unlike Lee and Thomas, they found considerable difference in the sex ratio, though the men tended to die younger, so that in middle age the ratio of male to female deaths was 5:1. Particularly interesting was the finding that in the highest social class the mortality from coronary disease was 10 times greater in the professional and business men than in their wives, indicating the strong influence of mental stress and strain. In their series, they were unable to relate coronary disease to smoking habits; Lee and Thomas, while agreeing in this respect, pointed out that the increase in tobacco consumption was followed by a lowering of the influence of sex, so that women appeared to be more liable to infarction as their smoking habits increased. Lee and Thomas were unable to relate infarction with the consumption of dairy products, though there was some increase in average fat consumption during the period of the series. They were not able to confirm the importance of socio-economic factors, though no detailed survey was made on this point. Thus in this recent series the increasing incidence of myocardial infarction is confirmed, as is the importance of *diabetes mellitus*. The explanation for the ironing out of the sex ratio is obscure. That the increasing incidence is a real one prompts further inquiry on this important problem.

A final interesting note is afforded by the recent study of O. Saphir, I. Ohringer and H. Silverstone[4] on the relative frequency of arteriosclerotic heart disease in the different age groups. The survey was based on the findings at the post-mortem examinations of several thousand subjects, over twenty years of age, between the years 1920 and 1953. No differentiation was made between the degrees of coronary arteriosclerosis or atheromatosis. In assessing the results of the survey, the authors took account of

[1] *Arch. Int. Med.*, April, 1956.
[2] *Arch. Path.*, August, 1949.
[3] *Circulation*, June, 1950.
[1] *Circulation*, April, 1950.
[3] *Ann. Int. Med.*, January, 1948.
[3] *Brit. Heart J.*, 11:4, 1949.
[4] *Am. J. M. Sc.*, May, 1956.

the considerable shift towards increasing average longevity in the later years. It then became apparent that the overall frequency of arteriosclerotic heart disease has not changed. The significant discovery was that the frequency of coronary artery disease was considerably increased in the younger age groups, especially the forty to fifty year old subjects. It would thus appear that the changing stresses imposed by modern life, whether dietary or otherwise, cannot themselves account for the disease of the coronary arteries, but may only exacerbate an inherent degenerative tendency.

SEROLOGICAL REACTIONS IN RHEUMATOID ARTHRITIS.

Since 1940 a number of investigations have been carried out on certain serological reactions in patients with rheumatoid arthritis. In the April number of *The American Journal of Medicine* there is a review editorial by W. Epstein and C. Ragan[1] on the present position of the tests, and there are two long articles on the tests and their clinical evaluation by A. S. Jacobson *et alii* and by M. Ziff *et alii*.[2]

Three serological test systems have been investigated, but each group of workers seems to modify the tests in various ways. In the simplest test (S.A.), several strains of group A hæmolytic streptococci are incubated with serial dilutions of the patient's serum and in saline solution. Macroscopic clumping of the organisms constitutes a positive reaction. More commonly used is the sensitized sheep cell test (S.S.C.) or some modification of it. In this test sheep red corpuscles, to which have been added non-agglutinating amounts of rabbit sheep cell antiserum, are incubated with serial dilutions of the patient's serum in saline solution. The reaction is positive when the quantity of the patient's serum necessary to agglutinate the treated sheep cells is less than sixteen times that necessary to agglutinate untreated sheep red cells. The test may be made more sensitive and selective if the naturally occurring sheep red cell agglutinins in the test sera are removed by absorption and if, instead of saline, sheep serum is used for diluting the test sera (S.E.A. test). The third test (F11) uses sheep red cells treated with tannic acid and coated with pooled human γ globulin. These are added to serial dilutions of test sera and a positive reaction occurs when there is maximal agglutination of the treated sheep cells by a dilution of at least 1:56 of the patient's serum.

None of these tests is of the nature of an antibody-antigen reaction and the mechanism is not thoroughly understood. It is assumed that the streptococci and the sheep red cells are inert carriers of some constituent of serum called the reactant, and the serum rheumatoid factor or reactor is in another fraction of the serum. One of the factors is contained in all sera, the other only in serum from a patient with rheumatoid arthritis.

Jacobson *et alii* investigated 1576 patients with various types of arthritis and found the following. (i) Of 331 patients, 62% with definite rheumatoid arthritis had positive reactions to the S.E.A. test and 69% of 180 of these patients positive reactions to the F11 test. (ii) Of patients with rheumatoid spondylitis alone or with rheumatoid arthritis or psoriasis with arthritis, 10% gave positive reactions to the S.E.A. test and 15% to the F11 test. (iii) Of patients with all other varieties of arthritis, 3% had positive reactions to the S.E.A. test and 5·9% reacted to the F11 test. (iv) Of patients with no joint complaints, 3% gave positive reactions to the S.E.A. test and 2% to the F11 test. The longer the duration of the rheumatoid arthritis, the more positive results there were, so that many early cases, in which diagnosis is difficult, are likely to be missed by these tests.

[1] *Am. J. Med.*, April, 1956.
[2] *Ibidem.*

Ziff *et alii* have demonstrated that in a proportion of cases of rheumatoid arthritis there is a substance in the serum which inhibits the tests. This effect can be largely overcome if the euglobulin fraction of the patient's serum is used instead of the whole serum. It is difficult to assess the value of these tests as routine procedures. In a high percentage of cases of rheumatoid arthritis, which are readily diagnosable, positive reactions are obtained, but in early cases in which the diagnosis is difficult the results of the tests may be negative, or positive results may be obtained with non-rheumatoid arthritis. The tests, too, are very complicated, and, as Ziff *et alii* state in commentary on a modification of the S.E.A. test, it is "a difficult technical procedure requiring considerable experience in reading agglutination tests". It seems that much more work requires to be done before the tests have much value in clinical medicine.

RHEUMATOID ARTHRITIS IN THE POPULATION.

Estimates of the prevalence of rheumatoid arthritis have varied considerably according to the method of examining or of questioning the population sample. Particularly in rheumatoid arthritis, the criteria for defining the disease are difficult, complaints of subjective sensations are unreliable, and diagnosis by clinical examination may be arduous and still indefinite. Even the reading of X-ray films presents difficulties in differences between observers and in individual observers at different times. J. H. Kellgren and R. Moore[1] suggested the name primary generalized osteoarthritis for a polyarticular form of osteoarthritis which is often confused with rheumatoid arthritis. Primary generalized osteoarthritis has distinct clinical and radiological features, which enable it to be distinguished from rheumatoid arthritis and from secondary degenerative osteoarthritis. The incidence of associated rheumatoid and primary generalized osteoarthritis was about 4%, but at this time it appeared that the incidence would be no more than that expected in a general sample of the population.

Help in the more exact diagnosis of rheumatoid arthritis can be obtained fairly simply by the application of a test involving the agglutination by the patient's serum of sensitized sheep's red cells. J. Ball[2] described a modified test of this kind in which the serum factor appeared to be highly specific for rheumatoid arthritis. In a large series of cases no positive results were obtained in the absence of arthritic disease and the percentages of positive results in ankylosing spondylitis, osteoarthritis, non-defined arthritis and rheumatoid arthritis were 2·4, 1·9, 7·8 and 91·5 respectively. Classification of rheumatoid from other arthritides in the many borderline cases was thus possible.

An estimation of the incidence of rheumatoid arthritis in a sample of workers was reported by Kellgren and J. S. Lawrence.[3] Diagnosis was made by means of a history, clinical examination and X-ray examination of the cervical and lumbar parts of the spine, the right knee and the right hand, and in each case the emotional stability of the subjects was estimated by means of psychometric tests. The subjects were all between forty and fifty years of age. Coal miners were found to have significantly more degeneration of the lumbar disks and more osteoarthritis of the knees than other manual or office workers. Pain was connected not with the relative emotional stability of the subject, but with the actual degree of arthritic changes. In an epidemiological study of rheumatoid arthritis in coal miners W. E. Miall[4] and other members of the Pneumoconiosis Medical Panel and Research Unit in Cardiff were able to show that rheumatoid arthritis was associated with characteristic changes in the radiological appearance of the chest. An appearance of wide-

[1] *Brit. M. J.*, January 26, 1952.
[2] *Lancet*, November 11, 1950.
[3] *Brit. J. Indust. Med.*, July, 1952.
[4] *Brit. M. J.*, December 5, 1953.

spread nodular fibrosis distinct from the usual progressive massive fibrosis of pneumonokoniosis was encountered in the examination of a large group of coal miners. Evidence suggested that the ætiology of the condition was similar to that of progressive massive fibrosis, but the nodular fibrosis seemed to develop at an earlier stage in the pneumonokoniosis, and it was suggested that this change was one of a particularly sensitive tissue reaction to dust and tuberculosis. In over 50% of the men with nodular fibrosis there was also radiological evidence of rheumatoid arthritis, while in the more typical progressive massive fibrosis the incidence of rheumatoid arthritis was only 3%.

Kellgren and Lawrence[1] have now made an estimate of the incidence of rheumatoid arthritis in the general population. The population studied was that of a small industrial English town of 48,000 inhabitants. One house was visited in every ten, and in 1949 to 1950 the age group of fifty to fifty-nine years was specifically studied. The survey was repeated in the same subjects five years later. In each case a history was taken and the small joints and spine were examined and notes were made of the subject's mental state. The differential sheep agglutination test, described by Ball, was performed; radiographs were taken of the hands, feet, knees, pelvis, and lumbar and cervical parts of the spine. Records were completed over the whole survey for 380 persons. Of the men 18% and of the women 48% had clinical evidence of polyarthritis of one kind or another; the incidence of clinical rheumatoid arthritis was 3% and 11% respectively. Positive results were obtained to the agglutination test in 5% of the men and in 6% of the women. Great care was taken to use standardized methods in the reading of skiagrams. On the results of these radiological tests, 8% of the men and 10% of the women were found to have changes consistent with a diagnosis of rheumatoid arthritis. It was noted incidentally that osteoporosis of the hands was almost confined to the women. Of the 283 persons with no clinical evidence of rheumatoid arthritis, definite serological or radiological signs of the disease were found in 20. It was considered that, except in the severe cases, the association between clinical diagnosis and the serological and radiological findings was poor. Only one-quarter of the women with osteoporosis of the hands had any real evidence of rheumatoid arthritis. The association between subjective morning stiffness and early rheumatoid arthritis was found to be slight, so that this cannot be used as a useful screening test, at least in the older subjects. Features such as cold, blue extremities, sweating, and tender nodules were associated with rheumatoid arthritis, but were relatively uncommon and so not particularly helpful in the reaching of a diagnosis. The two surveys conducted reveal a wide discrepancy between the diagnosis of rheumatoid arthritis in early and mild stages on clinical grounds, and on serological and radiological evidence. Moreover, during the five years there was a good deal of clinical variation in the mild cases between the two surveys. Little doubt was raised by the severe cases of rheumatoid arthritis, but as the majority of cases come from the less certain groups with some failure of correlation between the different methods of diagnosis, it is seen that estimates of the incidence of rheumatoid arthritis are fraught with complications, not least by the intrusion of polyarthritis of non-rheumatoid type. Kellgren and Lawrence maintain their opinion that clinical rheumatoid arthritis is three times as common in women as in men, but the results of serological and radiological tests in this survey were positive in equal numbers of the sexes. Especially of note were the 20 cases of rheumatoid disease with no clinical signs. This may in part have been due to the rheumatoid arthritis commencing, as it so often does, in the central rather than in the peripheral joints. Radiological signs of polyarticular osteoarthritis were found more frequently in men than in women. In this particular population sample, the prevalence of severe rheumatoid arthritis was 1% in men and 3% in women, while for all grades of clinical rheumatoid disease it was 11% in men and 27% in women. As Kellgren and Lawrence point out, this incidence cannot be applied to the general population, but only at the most to groups similar to this selected sample. The most important parts of this survey are the demonstration of the difficulties encountered in the diagnosis of mild rheumatoid arthritis, in its differentiation from other polyarthritic conditions, and in the wide discrepancies and limitation of diagnosis on clinical grounds.

[1] *Ann. Rheumat. Dis.*, March, 1956.

SKIN HISTAMINE.

THE skin of an average man weighs about four kilograms and contains about 30 milligrammes of histamine. There are wide differences between the amounts of histamine per gramme of skin in different animals and in different parts of the body of the same animal. It is highest in rats, then cats, then dogs and man, and very low in guinea-pig skin. The skin of the nose and extremities contains more than the skin of the trunk. Histamine liberators like the drug "48/80" release 90% of the histamine in the rat skin but virtually none from the guinea-pig. Man is intermediate. In a symposium on histamine, published by the Ciba Foundation, W. L. M. Perry considers the relation between the histamine content of the skin and reaction to allergies and anaphylaxis and the triple response. Skin allergic reactions are notoriously difficult to produce in the rat, but easy to produce in the guinea-pig. They will release histamine from the rat skin, but not, in significant amounts, from the guinea-pig skin. Skin allergic reactions are not affected by depletion of histamine in the rat to 10% of normal and antihistamines do not block allergic responses in the rat skin. Perry and his co-workers are of the opinion that histamine is not involved in the direct pathway of events leading to the antigen-antibody reaction in the skin. Histamins is released in this reaction, but the release is a side reaction or a result of the skin lesion and not the cause of it. Animals can be divided into three groups according to the skin content of histamine and their active and passive allergic reactions. The third group in Perry's classification include those animals which show the triple response—dog, ferret, pig and man. They have skin histamine levels intermediate between the other two groups. If the triple response is caused by histamine release, mere quantity of histamine is not the operative factor—there must be some other factor which determines its occurrence. The second group—guinea-pig, rabbit, monkey—show no triple response, but do show a high degree of active allergy in the skin. They all have low skin levels of histamine. The first group—mouse, rat and cat—have a very high skin content of histamine, complete or nearly complete absence of active allergic responses in the skin and no triple response. Perry suggests as a result of the foregoing considerations that there are at least two kinds of skin histamine, releasable and non-releasable. Releasable histamine, as has been shown by J. F. Riley in a paper in the same publication, is located in basophile mast cells. All species have non-releasable histamine in their skins and its concentration is almost constant. Releasable histamine is not responsible for the triple response. What the non-releasable histamine does is not known. In the same publication there are two papers, one by W. E. Brocklehurst and the other by H. O. Schild, on a substance of unknown nature which is set free in certain if not all tissues when an antigen-antibody reaction takes place. This has been called "SRS-A", slow reacting substance in anaphylaxis, and it can be revealed in perfusates by suppressing the histamine with large doses of an antihistamine, mepyramine. This substance causes contractions in guinea-pig intestine. It differs pharmacologically from bradykinin and 5-hydroxytryptamine. It appears to be of importance in human asthma, but whether it appears in the skin has not yet been demonstrated, and it is not yet known what is released in the skin to cause the allergic reaction lesions.

Abstracts from Medical Literature.

THERAPEUTICS.

Penicillin in Late Patent Syphilis.

M. L. NIEDELMAN (*Arch. Dermat.*, May, 1956) has made a study to determine the therapeutic value of penicillin in late latent syphilis as estimated by the outcome of serological tests. On the basis of recent reports, he suggests that late latent syphilis comprises more than half the total syphilis cases reported. Late latent syphilis is defined as asymptomatic syphilis of more than four years' duration, with no clinical or laboratory evidence except a positive result to a serological examination. A normal cerebro-spinal fluid was required in all patients before late latent syphilis was diagnosed. It has been variously estimated that late complications may develop in syphilis in from 25% to 35% of untreated patients. A total number of 316 patients were studied. Serological tests were performed for from one to three years after the initial treatment. Procaine penicillin G, containing 2% aluminium monostearate in sesame oil, was used throughout the trial. The majority of the patients were female, and the most satisfactory results to treatment were obtained in the younger age groups. The best results were obtained in those patients who had had previous adequate bismuth and arsenical therapy; the poorest results were obtained in patients previously treated with penicillin. Penicillin was found to be effective in the ultimate results of the serological examinations for late latent syphilis, as were arsenic and bismuth. When the patient's titre remained at a satisfactory level of from four to eight Kahn units, no amount of retreatment was found to alter the titre. Therefore, if a patient was retreated once, this was sufficient to attain the desired end results. The penicillin resulted in lower titres both in formerly treated and in untreated patients. No progression of the disease occurred in this series of cases.

Spiramycin.

D. G. HUDSON, G. M. YOSHIHARA AND W. M. M. KIRBY (*Arch. Int. Med.*, January, 1956) have made a study of spiramycin, a new antibiotic produced by a strain of streptomyces isolated from soil samples in France. It was found that pneumococci, streptococci and staphylococci were inhibited by low concentrations of the antibiotic *in vitro*, but they were, in general, less sensitive than to penicillin or erythromycin. Of particular interest was the fact that most strains of staphylococci, resistant to penicillin or erythromycin, were sensitive to spiramycin. As compared with erythromycin, however, the usefulness of spiromycin in the treatment of staphylococcal infections may be limited by the fact that the staphylococci are less sensitive *in vitro* to spiramycin, and larger amounts are required to produce equivalent blood levels. Spiramycin was found to be well absorbed when administered by mouth in doses of one gramme every six hours. The antibiotic was well tolerated. Some patients complained of the bitter taste, and two patients had diarrhœa, which was possibly caused by the antibiotic. Favourable therapeutic results were obtained in a group of 29 patients with bacterial pneumonia. Twenty-six patients were afebrile within five days and made an uneventful recovery. Two patients ran a more prolonged febrile course and one patient with Friedländer's pneumonia failed to respond.

Overdoses of Pentylenetetrazole and Barbiturate Combinations.

J. F. FAZEKAS, L. R. GOLDBAUM, T. KOPPANYI AND J. G. SHEA (*Am. J. M. Sc.*, May, 1956) have made a study of the relative human toxicities of combinations of pentylenetetrazole with pentobarbital sodium, secobarbital sodium and phenobarbital sodium respectively. The duration of action of these combinations was evinced by the clinical signs and the blood levels obtained in human volunteers. Also studied was the protective effect afforded by pentylenetetrazole in these combinations. In addition, large doses of pentobarbital sodium alone were administered to a control group of volunteers to illustrate more clearly the magnitude of the protective action of pentylenetetrazole when taken simultaneously with barbiturates. The ingestion of from 1300 to 2000 milligrammes of pentobarbital sodium, simultaneously with three times the amount of pentylenetetrazole, produced neither anæsthesia nor severe central depression in human volunteers. The ingestion of from 800 to 1000 milligrammes of pentobarbital sodium alone, however, resulted in most cases in marked central nervous system depression and, in the majority of cases, in light surgical anæsthesia. Pentobarbital sodium was absorbed more rapidly from the gastro-intestinal tract than fixed mixtures of pentobarbital sodium and pentylenetetrazole. The rate of disappearance of pentobarbital from the blood was the same in both groups, approximately 1·5% of the ingested dose per hour. Subjects ingesting secobarbital sodium in doses from 1300 to 1500 milligrammes, with three times the amount of pentylenetetrazole, showed no signs of marked barbiturate depression. The rate of fall of the blood levels was approximately 2·5% per hour. Subjects ingesting phenobarbital sodium in doses of from 2000 to 4100 milligrammes with one and one-half times as much pentylenetetrazole were only sedated and could easily be aroused. The rate of disappearance of this barbiturate from the blood was approximately 0·7% per hour. Many subjects who took the barbiturate-pentylenetetrazole combinations vomited, indicating denarcotization of the vomiting mechanism. The control experiments, as well as the review of the pertinent literature, indicate that pentylenetetrazole is an efficient preventive when taken simultaneously with coma-producing or possibly fatal doses of barbiturates. Pentylenetetrazole given in these combinations, and in the above stated dose ranges, did not produce convulsions. Therefore, in the human, under the above conditions, pentylenetetrazole and barbiturates are mutually antagonistic.

Acenocoumarin, a New 4-Hydroxycoumarin Anticoagulant.

F. J. SHILLING AND O. R. KREUSI (*Am. J. M. Sc.*, May, 1956) have described the characteristics of acenocoumarin, after the investigation of its clinical application as an anticoagulant. Sixty-five patients treated with the anticoagulant were observed daily for an average period of twenty-seven days and the results of the trial represent the clinical evaluation of the drug. Effective drug doses were found to be 20 milligrammes on the first day, eight to 16 milligrammes on the second day, and an average of four to six milligrammes for maintenance therapy. Vitamin *K* appears to be effective in reversing excessively prolonged prothrombin times due to acenocoumarin, as with other coumarin anticoagulants. This particular anticoagulant appears to have certain advantageous characteristics. These features are: the effectiveness in small, single, daily oral doses; the absence of untoward side effects; and the ease and safety of maintaining therapeutic anticoagulation.

Acetyl-Digitoxin.

I. C. BRILL, P. R. BURGNER AND N. A. DAVID (*Ann. Int. Med.*, April, 1956) describe how acetyl-digitoxin, derived from enzymatic cleavage from lanatoside A, has been employed, given by mouth, in the treatment of various types of heart disease. Twenty-six hospital patients were initially digitalized with this drug, and a group of 46 ambulatory patients, previously digitalized by other preparations, were placed on maintenance therapy. Because acetyl-digitoxin has a short latent period, with rapid onset of action, it was found useful for rapid digitalization; it was given in divided doses, 0·8 milligramme initially, followed by two 0·4 milligramme doses given at two-hour intervals. The results were carefully noted by clinical and electrocardiographic observations. In most cases, a total of 1·6 milligrammes of acetyl-digitoxin effected satisfactory digitalization within six to eight hours of the start of therapy. Few toxic or untoward reactions were encountered, and such as appeared were readily reversible by discontinuing the medication for twenty-four to forty-eight hours. Nausea and vomiting, when they occurred, were generally seen within an hour or two of administration of a full digitalizing dose of the drug, while arrhythmias, when noted, usually occurred several hours later. Thus the more serious toxic effects of acetyl-digitoxin may be prevented by discontinuing the drug upon the appearance of nausea and vomiting. For maintenance, an average dose of 0·15 milligramme of acetyl-digitoxin per day was found most satisfactory.

Neuromuscular Block in Man.

H. C. CHURCHILL DAVIDSON (*Anesthesiology*, January, 1956) describes the types of neuromuscular block which occur in man, and divides them into four groups.

A deficiency block is caused by any factor which interferes with the liberation of acetylcholine; for example, procaine, botulin toxin, or calcium deficiency. A depolarization block is similar to that produced by acetylcholine in normal neuromuscular transmission, but there are increased duration and extent of the depolarization. Decamethonium and succinyldicholine belong to this group. Decamethonium is not hydrolysed *in vivo* and is excreted unchanged in the urine. Succinyldicholine is rapidly hydrolysed by plasma to succinylmonocholine, and then to succinic acid and choline. Muscle fasciculations occur with this group. Decamethonium produces a characteristic tightness of the jaw and calf muscles soon after the injection, and this may persist for some hours. Succinyldicholine gives brief widespread fasciculations, more marked after rapid injections, and may cause muscular stiffness the following day. Electromyelography reveals that these twitches are not single muscle fibre potentials, but are full action potentials representing a whole motor unit of 150 to 300 muscle fibres contracting simultaneously. This is called the Masland-Wigton phenomenon, and is presumably due to an antidromic reflex. The term non-depolarization block is preferred by the author to that of competitive inhibition block, because both these groups compete with acetylcholine for the end-plate receptor. Curare combines with the receptor protein without causing depolarization, thereby stopping the normal acetylcholine from producing depolarization and muscular contraction. If the concentration of acetylcholine can be raised by inhibiting the action of choline-esterase with neostigmine or "Tensilon" to a level at which the excitation threshold of the end-plate is reached, then the neuromuscular block is overcome. Dual block occurs in cases of *myasthenia gravis* and in certain circumstances after the administration of succinyldicholine and decamethonium. Reevaluation of the sensitivity to the tubarine test for myasthenia has shown that only those muscles which are clinically weak possess this hypersensitivity, whilst other muscles give a normal response, so that it is unlikely that the respiratory function will be affected during this test. Normally three milligrammes of decamethonium produce profound muscular weakness, and, if an anticholinesterase drug is then given, there is a severe increase in the weakness. In myasthenia, the response to decamethonium varies with the degree of weakness clinically present. A patient with a mild form of the disease and symptoms limited to her eyelids, had no sign of paralysis after the administration of 10 milligrammes of decamethonium. This resistance to decamethonium illustrates the generalized nature of the disease, and if an increasing dose of the drug had been injected into this patient, the eyelids would be paralysed first. A patient with severe myasthenia had paralysis after the administration of 1·5 to 2·0 milligrammes. Nevertheless, in myasthenia the paralysis produced by decamethonium is not a depolarization block but a curare-like block, and is readily reversible by neostigmine or "Tensilon". The brief period of depolarization precedes the change over to the non-depolarization block. These two types of block may explain the different reactions of curare-like drugs in animals, and also some cases of prolonged apnœa. The authors summarize the causes of prolonged apnœa. The central causes are an overdose of the anæsthetic and premedicant drugs, or an alteration in the plasma carbon dioxide level. The peripheral causes are several. A relative overdose of the relaxant may occur because of the poor mass of muscle in the particular patient, the state of the circulation and renal secretion, and the presence of hypotension and hypothermia; in practice these last three play little part. Summation of drugs, for example ether and tubarine or decamethonium and "Prostigmin", may cause relative overdosage. Accumulation of succinylmonocholine would occur only with continuous succinyldicholine in the presence of low pseudocholinesterase, as in liver disease, under conditions of nutritional cachexia, after the administration of anti-cholinesterase drugs, and very occasionally in otherwise normal people. Dual block occurs in *myasthenia gravis* or under persistent bombardment with a depolarization drug, and is reversible by neostigmine. In the diagnosis of the causes of prolonged apnœa the following suggestions are made: electrical stimulation of the main nerve to a muscle group; measurement of plasma carbon dioxide levels and cholinesterase levels; and a trial injection of 10 milligrammes of "Tensilon". If a dual block is present, muscle tone will return, but if a depolarization block is the cause of the prolonged apnœa, the worsening effect of the "Tensilon" will be brief.

NEUROLOGY AND PSYCHIATRY.

Pregnancy Experience and Behaviour Disorder in Children.

B. PASAMANICK, M. ROGERS AND A. LILIENFELD (*Am. J. Psychiat.*, February, 1956) state that the prenatal and paranatal records of children with behaviour disorders, born in Baltimore after 1939, show significantly more complications of pregnancy and delivery and prematurity than their matched controls. The non-mechanical abnormalities, such as toxæmia, appear to be the important factors in this association rather than the mechanical factors of delivery. These associations are present even when intellectual and environmental factors are controlled. Hyperactive, confused and disorganized children have even more of these abnormalities in their backgrounds. An hypothesis of a continuum of reproductive casualty is formulated, consisting of brain damage incurred during these periods, leading to a gradient of injury extending from fœtal and neonatal death, through cerebral palsy, epilepsy, mental deficiency and behaviour disorder.

Cortisone and Hydrocortisone in Pia-arachnoid Adhesions.

S. FELDMAN, A. J. BEHAR AND M. SAMUELOFF (*Arch. Neurol. & Psychiat.*, December, 1955) have studied the effect of intracisternal injection of cortisone and hydrocortisone on the formation of talcum-induced pia-arachnoid adhesions in cats. In the non-treated animals dense adhesions were formed. Repeated intracisternal administration of cortisone and, especially, of hydrocortisone at intervals of two or three days in 25 animals decreased mainly the migration and phagocytic activity of the histiocytes in the subarachnoid space. They thus inhibited the formation of foreign-body giant-cell granulomata, which formed the pia-arachnoid adhesions in the non-treated animals.

The Autistic Child in Adolescence.

L. EISENBERG (*Am. J. Psychiat.*, February, 1956) states that the two cardinal symptoms presented by the autistic child are self-isolation present in the first years of life, and the obsessive insistence on the preservation of sameness. Of the cases selected for study, all the children had distortion of language function. This ranged from mutism, delayed onset in speech, echolalia, affirmation by repetition and prenominal reversal, to a highly metaphorical language with little intent to communicate meanings to others. Sixty-three autistic children were evaluated at a mean age of fifteen years after a mean follow-up period of nine years. Almost one-third achieved at least a moderate social adjustment. The prognosis was shown to vary significantly with the presence of useful speech at the age of five years, taken as an index of the severity of autistic isolation. Half of those who possessed meaningful language by the age of five years improved, whereas only one of 31 children without the ability to communicate verbally by that age, had shown significant improvement. The clinical course of these children justified the segregation of early infantile autism as a clinical entity, probably to be included within the group of schizophrenias. The psychopathology of autism is reviewed and the suggestion is offered that the fundamental feature is a disturbance in social perception.

Preadolescent Schizophrenia.

F. J. KALLMAN AND B. ROTH (*Am. J. Psychiat.*, February, 1956) state that since most schizophrenic psychoses manifest themselves only after adolescence there must be important factors that may lead to recognizable symptoms before the age of fifteen years. The crucial point in diagnosis was a distinct change in behaviour of a child who previously seemed to be developing normally. The most frequent symptoms were diminished interest, blunt or distorted affect, peculiar conduct, especially in motor activity, diffuse anxiety with phobias, vague somatic complaints, exaggerated fantasies and hallucinations. The authors investigated 52 twins and 50 single children under fifteen years of age. No ætiological significance was detected either in the birth order of the child or in the age of the parents. There was a definite excess of males over females in the preadolescent group. Their findings indicate the early effect in childhood schizophrenia of the same genotype (gene-specific deficiency state) assumed to be responsible for the basic symptoms of adult schizophrenia.

Medical Societies.

PÆDIATRIC SOCIETY OF VICTORIA.

A MEETING of the Pædiatric Society of Victoria was held at the Royal Children's Hospital, Carlton, Victoria, on December 14, 1955.

Neuromyelitis Optica.

DR. E. G. ROBERTSON presented the clinical details of a female patient, aged fifteen years, suffering from *neuromyelitis optica*. He said that on January 19, 1955, a previously healthy girl of fourteen years had noticed, while swimming, that the water on her legs seemed unduly cold and her legs felt somewhat weak. During the next day she was unable to pass urine or fæces, and she felt some abdominal pain. She went for a long walk on that day, and in the evening her feet felt numb and tingling. Subsequently weakness of the lower limbs rapidly increased until seven days after the onset she had no voluntary power over the lower abdominal muscles and the lower limbs. The deep reflexes in the lower limbs became less active over that period, the muscles becoming flaccid. The abdominal reflexes were absent and the plantar responses extensor at an early stage. Superficial sensibility was diminished below the eleventh thoracic dermatome on the third day of onset, with a zone of over-sensibility above. Appreciation of position and passive movement and vibration were less involved early, but later became increasingly impaired, while the level of impairment of appreciation of pin-point and heat and cold (while being greatest over the left lower limb) rose to the fifth thoracic dermatome. Appreciation of light touch was slightly reduced. There was no headache, fever or pain. Intermittent catheterization of the bladder (later replaced by tidal drainage) and enemata were necessary.

Forty-eight hours after the onset of the condition, the cerebro-spinal fluid, which was under a normal pressure, contained six lymphocytes and two polymorphonuclear cells per cubic millimetre. Four days later the pressure was 50 millimetres of fluid and the response to jugular compression was brisk and full. The lymphocytes increased in number to 19 per cubic millimetre. The protein content was 30 milligrammes, the chloride content 730 milligrammes and sugar content 0·04 milligramme, in each case per 100 cubic centimetres. The colloidal gold curve was normal, and the Wassermann reaction was negative. The findings of X-ray examinations of spine and chest were normal. The patient had an unhealed sore on the right foot, which had been present since a minor injury three weeks before the onset, and the possibility of compression of the spinal cord by an extradural abscess prompted myelography. The opaque material flowed freely up and down the spinal theca. She was treated with ACTH for two and a half weeks and with penicillin (and later with a series of antibiotics such as were indicated by changing sensitiveness of the *Bacterium coli* and *Proteus* grown from the urine).

Nineteen days after the onset extensor tone was returning to the still paralysed lower limbs. As the deep reflexes gradually increased, clonus could be elicited, and plantar stimulation produced a flexion response of the corresponding lower limb, the toes and feet strongly dorsiflexing.

Four weeks after the onset hypalgesia increased, and over the next week appreciation of light touch became reduced. Some fever, apparently due to urinary infection, persisted throughout this period. The picture at the time was one of complete transverse myelitis. The cellular content of the cerebro-spinal fluid was normal. The previously introduced "Myodil" flowed freely throughout the spinal theca.

Two months after the onset of illness the patient began to move her thighs and flex the toes of the right foot. During the next week power and sensation rapidly improved, and she regained the recently lost sensory perception. Tidal drainage was continued except for short trial periods. After involuntary evacuation, which could be stimulated by repeated abdominal pressure, there was a large volume of residual urine. About that time she was transferred to Frankston Orthopædic Branch for convalescence.

DR. D. GAILBRAITH then gave a short account of her progress at that hospital. He said that the motor power in the upper extremities appeared to be normal, but the power of all movements of the lower extremities was decreased. Her legs could just be raised against gravity, the left side being weaker than the right. However, bladder and bowel control was practically absent. From that time on, the return of motor power was slow but steady. Urinary infection was gradually controlled and partial control of the bladder regained. Bowel control was regained more quickly.

Four and a half months after the onset she was able to walk with a nurse alongside her, but evidence of a bilateral upper motor neuron lesion remained, being greatest on the right side.

Four months after the onset (on May 12), during the stage of improvement of the spinal lesion, she noticed rapid loss of central vision of the right eye, which increased to almost complete blindness. The eye was tender to pressure and on movement. The vision was reduced to perception of hand movements in the peripheral parts of the field, and there was a large dense central scotoma. The optic disk appeared normal, but later slight blurring of the edges was seen. Two weeks later the scotoma was slightly smaller.

About seven weeks after that episode (on July 3) she noticed that she could not see print clearly with the left eye. There was no pain on movement or pressure, and the optic disk appeared normal. Cortisone, in a dosage of 25 milligrammes eight-hourly, was prescribed, and on the next day was increased in amount to 300 milligrammes each twenty-four hours. Later, ACTH was added. During the next few days the vision of the left eye deteriorated, with the appearance of a central scotoma. On July 21 the vision of the left eye was noted to be improving. On July 28 the visual acuity was 6/6 (Snellen), and the scotoma had disappeared. The vision of the right eye commenced to improve later than that of the left. Administration of cortisone was discontinued on October 18 (9325 milligrammes having been given) and of ACTH on November 4 (after 1000 units had been given).

Meanwhile, the function of her lower limbs improved until her gait became almost normal. Residual weakness of dorsiflexion of the left ankle and toes suggested lower motor neuron involvement. The sensory loss disappeared.

A short film showing the girl's present state of well-being and activity was then shown.

Dr. E. G. Robertson then gave a summary of her condition at the present time. He said that the visual acuity of each eye was 6/6, and the visual fields were full, although she noticed that her colour vision was not quite as good as before. The deep reflexes were absent and the plantar responses briskly extensor.

Summarizing the case, he said that the patient was a girl of fourteen years who had first noticed slight sensory disturbance over the lower limbs, followed by retention of urine and rapidly increasing flaccid paraplegia, complete by the seventh day. The abnormal superficial reflexes showed it to be due to a lesion of the pyramidal tracts in the mid-thoracic region of the spinal cord. Later, tone increased in the extensor muscles. Appreciation of pain and temperature were impaired below the eleventh thoracic dermatome at an early stage, while light touch remained remarkably preserved. Conduction in the posterior columns was unimpaired. A band of hyperæsthesia, marking the upper level of sensory involvement, rose to the fifth thoracic dermatome over a few days, and thereafter sensory impairment remained stationary, until four weeks after the onset all forms of sensation over the lower half of the body were abolished. Gradual improvement commenced two months after the onset; and seven months after the onset little evidence remained of the lesion of the spinal cord, save for briskly extensor plantar responses.

Four months after the onset optic neuritis produced a large central scotoma in the right eye, and seven weeks later the left eye became similarly involved. Vision returned almost to normal over the next five months.

Dr. Robertson said that the association of involvement of the spinal cord and of the optic nerves had been known for a long time, but papers by Devic in 1894 and 1895 had served to define a group which he called *neuromyelitis optica*. Erb, however, had described an earlier case in 1879. The term, it would be noted, was purely topographical. It said too much and yet too little, and the term neuromyelitis was tautological. The literature conveyed an impression of bad prognosis, perhaps because Beck, in describing the clinical and pathological features of a relapsing case of his own, had collected 70 cases and boldly and somewhat ambiguously stated that "only seven showed a definite abatement or amelioration during the progress of the disease. On the other hand, the remaining cases either gradually or quickly but always more or less steadily, progressed to a certain stage, and the illness then resulted in either arrest or death. Many of the patients who survived made good recoveries, but some remained more or less stationary". The tendency

to report cases with pathological confirmation had undoubtedly given the disease a very bad reputation.

In Beck's series myelitis had preceded ocular signs in 36 cases, and the reverse had occurred in 18. In 10 the two had appeared together, and in four there was no complaint of visual failure, the ocular signs being found on routine examination. Days or weeks might elapse between the development of the various signs. The myelitis produced atonic or spastic paraplegia, nearly always progressive. The ocular symptom was sudden loss of vision due to a central scotoma or some form of hemianopia. There was at the most slight papillitis, and optic atrophy developed.

Dealing with the ocular manifestation of *neuromyelitis optica*, Lindsay Rea had stated that bilateral central scotomata appeared rapidly and proceeded to complete blindness, and vision might just as rapidly recover. McAlpine had said that the prognosis depended upon which of three groups the cases fell into: some patients died acutely, others died of the effect months later, a relatively small number appeared to recover, usually with some residual effects.

The pathological lesion was like that of disseminated sclerosis, although it was said by some that there was a much greater tendency to destruction of axis cylinders in *neuromyelitis optica*. Briefly stated, microscopic examination showed patchy demyelination, chiefly around vessels, with perivascular infiltration of lymphocytes and fewer polymorphonuclear cells. When the lesion was severe, axis cylinders suffered destruction; when it was slighter, preservation of the axis cylinders allowed varying degrees of recovery. In the acute stages scavenger cells laden with debris were seen; in late stages glial proliferation had led to sclerosis.

It had been contended that the disease was a form of disseminated sclerosis, and chance might well determine such a localization of incidence in a certain percentage of cases. Some cases diagnosed as *neuromyelitis optica* had been found at autopsy to be instances of disseminated sclerosis.

Reports by Miller and by Miller and Gibbons had recorded considerable improvement in seven of ten patients suffering from acute disseminated encephalomyelitis during five-day courses with ACTH and no change in patients suffering from exacerbations of disseminated sclerosis. Glasser and Merritt had found transient improvement during fourteen days' treatment in chronic cases of disseminated sclerosis. Miller, after treating seven patients with the former condition, had stated that he was well aware that acute disseminated encephalomyelitis had a pronounced tendency to rapid, spontaneous and often complete recovery, and believed that the results were suggestive enough to warrant further trial. In the first article he had said that the treatment could at least do no harm. In the second paper, written with Gibbons, the report had been much more optimistic, although in one of the three added cases the patient died. Scott was stated by them to have caused improvement in sufferers from the after effects of *neuromyelitis optica* by administering ACTH. However, Dr. Robertson could find no reference to that in the article cited. Scott had described 10 cases characterized by severe optic neuritis and myelitis.

Miller and Gibbons had stated that they considered *neuromyelitis optica* a variant of acute disseminated encephalomyelitis. It was extremely difficult to assess the result of treatment in diseases which might remit. A very large series of cases would be necessary before any conclusion could be reached.

Thus the diagnosis of *neuromyelitis optica* had no true scientific basis. The term was purely topographical, and different ætiological agents might be involved. The clinical course was very variable, although the mode of onset gave a uniformity to the group. It was generally held that the progressive nature of the disease, the gravity of the myelitis and the bilateral optic neuritis, with little tendency to remit, helped to distinguish the disease from disseminated sclerosis. Further, the colloidal gold curve was usually normal in *neuromyelitis optica*. There might be slight lymphocytosis. The present case was typical of a number which he would place in that group. Some years previously in one evening he had shown to the Society two children who had recovered remarkably fully. Others seen subsequently had followed a similar course. A remarkable feature in several cases had been the contrast between good visual recovery and the whiteness of the optic disk. Chance coincidence not infrequently misled, but it was not unfair to state that the outlook in such cases was not invariably bad. Excellent recovery of power and vision was possible. Further, no relapses had occurred in those cases after recovery, which seemed to weigh against *neuromyelitis optica's* being a form of disseminated sclerosis.

DR. H. WILLIAMS asked Dr. Robertson whether the introduction of "Myodil" into the spinal theca had ever been known to cause relapse in the condition.

Dr. Robertson said that it had not, although he was very chary of using it in any inflammatory or other condition, and he usually removed it after the test.

DR. ELIZABETH TURNER cited a patient who had been in the Children's Hospital in 1946 at the age of five years with complete paraplegia and bilateral central scotomata, and said that the patient was now completely normal and had not had any recurrences.

The Use of Hydrocortisone for Eczema.

DR. A. DAY discussed the response to hydrocortisone acetate ointment in a group of cases of infantile eczema and other dermatoses. He said that hydrocortisone was said to exert an anti-inflammatory and anti-pruritic effect when applied locally, but not to be absorbed to an appreciable extent from local application, and in fact, its absorption after local application could not be demonstrated by Smith in 1953.

Sultzberger and Baen in 1953-1954 had stated that hydrocortisone acetate ointment offered a most important advance in topical dermatological therapy, and much had recently been written on its use.

It was therefore thought that some local investigation into its efficacy should be made, and with that in view a series of tubes containing the base only and the base with 1% of hydrocortisone was obtained. One series had a red label, and the other a blue, the actual contents being known only to the makers. The cases were typical of infantile eczema of a moderately severe type.

At first the patients were supplied with two tubes, one with a red label and the other with a blue label, with instructions that one should be applied to each side of the body—the red on the right side and the blue on the left.

However, it soon became obvious, from the improvement noted, that the red tube contained the active ingredient, and in most cases that was finally applied to all areas or used alone from the commencement.

In all the adult cases, hydrocortisone 1% in the same base, or in *Cremor Cereæ Sulphonatæ*, was used.

There were ten children with infantile eczema, ranging from two months to one year in age, six adult men with eczema, two with dermatitis of the hands and one with contact dermatitis.

A total of nineteen patients were treated with hydrocortisone. Of the ten children, one improved dramatically in forty-eight hours, six improved after about fourteen days and three did not improve in that time. All the adult patients improved. In all patients who improved the improvement was noticed very quickly, and in some it was dramatic and was maintained. But in the majority who improved the condition tended to recur on discontinuing the treatment.

Dr. Day said that his thanks were due to Upjohn, of England, who had generously made supplies available in different coloured tubes, but otherwise unlabelled.

He said that in view of the lack of proof of absorption, one adult case was interesting. The patient had had an intractable nummular eczema for many months, which did not respond to the usual application or to X-ray therapy, and had had no symptoms to suggest a fault in the function of any particular system. His rash cleared quickly, and he remained comfortable on treatment with hydrocortisone ointment (1%), but irritation and rash recurred if that was discontinued for a few days. He commenced the application in November, but about April noticed some slight digestive discomfort, which persisted. In June, on X-ray investigation, a medium-sized penetrating ulcer was demonstrated on the lesser curvature. He was put on an ulcer regime and the hydrocortisone was discontinued; he quickly lost all digestive discomfort, but the rash had recurred. He was now using a minimal amount of hydrocortisone and just holding the rash.

Dr. Day said that the conclusions drawn from the small series were that hydrocortisone in 1% strength applied topically allayed the local inflammatory reaction and irritation, and was invaluable in that it gave time for other measures to have been instituted and to take effect with possible cure.

Hydrocortisone, while acting on the cells in some manner to allay irritation and improve the resistance, was not a curative agent *per se*.

DR. D. HAGGER asked Dr. Day whether he could give any idea of the amount of hydrocortisone that was given to the man who developed an ulcer. Dr. Day said that he could not do so, but the man had a fairly generalized eczema and applied the ointment for about six months, although it was used sparingly as the treatment was expensive.

DR. M. POWELL asked whether there had been any series of cases of sufficient size studied during the use of oral cortisone therapy for infantile eczema.

Dr. Day said that the general opinion seemed to be that administration of cortisone by mouth was not advisable and not effective. He had had no success with it himself. By and large dermatologists were not using it by mouth.

DR. H. WILLIAMS asked whether any specific dietary measures were used for the children concerned, or whether they were fed as normal children.

Dr. Day said that the children were restricted a little in diet because he thought that most of the patients with infantile eczema were overfed. There were no specific restrictions, the diet being of normal composition.

DR. V. COLLINS said that he thought that there was some evidence that oral cortisone therapy was very helpful, and that had been reported from the Boston Children's Hospital. If it could be treated by giving no more than 75 milligrammes per day, then no undesirable effects resulted from prolonged use. Dr. Collins himself had had success with it and thought that oral cortisone therapy had transformed a mother's life in regard to infantile eczema. He thought that if one could use less than 75 milligrammes per day, it was probably more economical to use it that way than as an ointment. In milder cases, with just a few small areas affected, the ointment would perhaps be better.

DR. H. SINN asked whether Dr. Day had formed any opinion of the relative value of cortisone in the exudative type of eczema and the dry type.

Dr. Day said that he thought that the difference was only in acuteness of the reaction, and he did not call them different types. Cortisone could help calm down the acute reaction well.

DR. J. COLEBATCH supported Dr. Collins's view that oral cortisone therapy was effective in adequate doses and wondered whether the dermatologists used doses of sufficient size. He had found topical application very effective also, and thought that perhaps the reason for Dr. Day's having some failures was that he, as a dermatologist, received only the most difficult cases.

DR. D. HAGGER thought that local application was as effective and probably safer.

Dr. Day said that he wondered whether all the patients treated by pædiatricians as suffering from eczema were suffering from true infantile eczema. That might account for some of the differences of opinion regarding oral cortisone therapy.

Fœto-Maternal Transfusion: A Cause of Neonatal Anæmia.

DR. J. COLEBATCH discussed the condition of fœto-maternal transfusion in a paper by himself, Dr. David Pitt and Dr. T. G. Maddison, and cited it as a cause of neonatal anæmia in two cases from the Royal Women's Hospital (see page 209).

MISS BETTY WILSON then gave a commentary on the use of fœtal hæmoglobin estimations in this and other disorders. She said that it had been known for some time that the hæmoglobin pigment in the newborn differed from that of normal adults. That had been shown by various methods, but in 1951 Singer and Chernoff had devised a simple method for the detection of fœtal hæmoglobin which could be used in a routine laboratory.

Hæmoglobin was prepared from fresh oxalated or clotted blood obtained by venipuncture. A measured amount of this hæmoglobin was exposed to the action of sodium hydroxide with a pH of 12·7 for an exact period of time. The non-hæmoglobin chromogens were precipitated, and the unaltered hæmoglobin was estimated by means of a photoelectric colorimeter.

Most of the hæmoglobin present in the newborn was fœtal, and that was rapidly replaced by the adult pigment, but distinct amounts of fœtal hæmoglobin could still be found in normal healthy children up to the age of two years. The normal adult range was from 0 to 1·7%, and Singer considered that a reading of 2% could be found only once in 370 determinations.

Other conditions in which alkali-resistant hæmoglobin was present were Cooley's anæmia and sickle-cell anæmia.

In discussing Dr. Colebatch's paper, DR. F. FORSTER said that the obstetricians were grateful to the pædiatricians for drawing their attention to the syndrome. He referred to other causes of anæmia occurring during the neonatal period, and expressed the view that the syndrome discussed by Dr. Colebatch might be the cause of some fœtal deaths *in utero*. He thought that it might be worth investigating the mother's blood for fœtal hæmoglobin when such deaths occurred.

DR. R. A. BARTER said that it seemed remarkable that more bleeding did not take place from the maternal sinuses, and in view of the rarity of the condition, it seemed certain that very little bleeding did take place.

Both DR. KATE CAMPBELL and DR. ELIZABETH TURNER cited cases that they had met with in practice. In one of Dr. Campbell's cases the patient had presented the appearance of *asphyxia pallida*, but had behaved atypically. Dr. Turner's case had simulated the chronic stage of anæmia seen in *erythroblastosis fœtalis*.

DR. D. HAGGER asked Dr. Colebatch whether anything was known of the cause of the condition, and whether there was any relationship between bleeding in the condition and the seepage of blood from the fœtal to the maternal circulation in Rh sensitization.

Dr. Colebatch said that the reason why hæmorrhage occurred was not known, nor was it known whether it had anything to do with seepage in erythroblastosis. He knew that gross seepage could occur in Wiener's syndrome not necessarily associated with Rh sensitization, even when there was the necessary background for that. He cited a case report in that connexion in which there was reason to suspect erythroblastosis in an anæmic baby, but there were no antibodies in the mother's blood. During a subsequent delivery she showed a rise of antibodies.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE STATE OF THE SETTLEMENT ON NORFOLK ISLAND.[1]

[Extract of a letter from William Redfern to D'Arcy Wentworth.]

Norfolk Island,
Sept. 16th, 1807.

Dear Sir,

. . . . . .

I have also to entreat you will send me a little Tea and Sugar, if it be only enough for my own use as in fact I do not wish for much while it remains so dear. It were unnecessary to say more to you on the subject of Iron Hoops as I am confident you will not omit forwarding those you already advised me you had purchased. I could also wish you to procure me some paper and if any acct Books should arrive I hope you will not forget I am much in want of some. I shall feel myself obliged by your sending me some iron large enough to make axles and other necessary parts for one of our Timber carriages—In one of my former letters I solicited you to send me some Hops which I suppose must have escaped your recollection as you took no notice of it. I shall however beg leave to remind you of it.

Our last crop of maize though sometime ago abundantly promising, has fallen far short of general expectation, indeed so much so that at least two thirds of the quantity that might have reasonably been expected to be obtained in good condition, is rotten with mouldiness owing to the recent Rains and from the same cause the weeds have been so extremely luxuriant in growth as to completely smother the

[1] From the original in the Wentworth Papers in the Mitchell Library, Sydney.

greater part of the Corn planted in June and July: these circumstances conjointly have prevented many hogs from being fatted and consequently induced Captain Piper to issue a Mandate prohibiting Individuals from slaughtering Pork for any other purpose than that of immediate domestic consumption, until such time as Govt. can be sufficiently supplied which I believe will not be this season. The want of Pork has rendered Fowls, Ducks Etc. so very scarce that I have been unable to procure any for some time past for my own use. You will be able from this acct of our Island to form a tolerably accurate Idea of our present Situation. Let me entreat you to favour me with all the information you have been able to obtain relative to the coming out ex detention of Colonel Foveaux. His arrival here is expected with the utmost impatience being destined in the public opinion to bring the ultimate Fiat of Government respecting the fate of this Island. Do you think the evacuation will be total or partial! I should be glad to know your opinion of my success, if, as soon as I can settle my affairs I were to remove to Port Jackson, and what pursuits would be the most eligible. I hope you will answer this letter as pointedly as you possibly can.

I remain, Dr. Sir,
Yours obediently,
WILLIAM REDFERN.

Correspondence.

A DISCLAIMER.

SIR: It has been brought to my notice that an advertising letter using my name and a pamphlet purporting to contain "extracts" of a paper delivered by me to the Australasian Medical Congress in August, 1955, have been circulated by Andrews Laboratories, Proprietary, Limited.

At no time has this firm sought or obtained permission from me to use my name in this or any other connexion, nor had they authority to print the article in question.

I would be obliged if you would publish this disclaimer of any prior knowledge on my part of this advertising material.

Yours, etc.,
PHYLLIS M. ROUNTREE.

Fairfax Institute of Pathology,
Royal Prince Alfred Hospital,
Missenden Road,
Camperdown,
New South Wales.
July 24, 1956.

SYDNEY HOSPITAL REFRESHER WEEK.

SIR: Since my request to you to publish a notice of the Sydney Hospital Refresher Week, the Deputy Commissioner of Taxation has written stating that expenses incurred in attending this course will be allowed as deductions for income tax purposes (File No. AF.1865/Pt.2). It would add to the value of the notice if this item could be included.

Yours, etc.,
J. M. YEATES.

"Harley",
143 Macquarie Street,
Sydney.
July 30, 1956.

THE MEDICAL BENEFITS FUND OF AUSTRALIA AND SERVICES RENDERED IN PUBLIC WARDS OF HOSPITALS.

SIR: The recent statement by Dr. H. R. R. Grieve as chairman of the Medical Benefits Fund, speaking with reference to services rendered in public wards, that "the 90% rule has been approved by all competent authorities, including the British Medical Association", leaves the suspicious reader wondering exactly what is the 90% rule.

I say "suspicious" with especial reference to such statements as that attributed once in the Press to Sir Earle Page, then Minister for Health, to the effect that insured patients would now receive back 90% of the doctor's fees; many of us waited in vain then for an immediate denial by our Association that doctors' fees were in any way fixed by a government schedule.

Now Dr. Grieve is doubtless strictly correct within one usage of the term "90% rule", but there seems some danger that a wider meaning may be attributed to his above-quoted statement.

Many I know will join me in requesting an answer to the question: "What *is* the 90% rule approved by the British Medical Association and has the Council ever agreed to a fixation of doctors' fees in relation to a government schedule?"

Yours, etc.,
C. C. MCKELLAR.

"Harley",
143 Macquarie Street,
Sydney.
July 24, 1956.

SIR: Dr. McKellar has been good enough to forward me a copy of his letter to you of the 24th instant, in advance of publication.

The term "90% rule", for three years in general use, was believed to be known to every practising doctor. The rule means that a registered medical benefit organization is not permitted to pay a benefit for any scheduled medical service exceeding 90% of the fee charged. Failure to observe this rule may lead to the loss of a fund's registration.

The term as used in my letter could scarcely have referred to anything else.

Yours, etc.,
H. R. R. GRIEVE.

July 26, 1956.

NEW SOUTH WALES BRANCH BALL.

SIR: Encouraged by the success of the Congress ball held last year, the Council of the New South Wales Branch of the British Medical Association decided some time ago to hold a ball at the Trocadero, George Street, Sydney, at 9 p.m. on Tuesday, September 4, 1956.

It is hoped to make the ball one of the outstanding social events of the year.

I would appeal to all members to do their best to be present at the ball and to bring their friends with them. A large attendance will ensure the success of the ball.

Tickets may be obtained upon application to the Medical Secretary.

Yours, etc.,
EDGAR THOMSON, President.

British Medical Association House,
135 Macquarie Street,
Sydney.
August 1, 1956.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Subscription Course.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that the following lecturers will be visiting Sydney during September and October, 1956.

Professor L. J. Witts, M.D., M.A., D.M., F.R.C.P., Nuffield Professor of Clinical Medicine, Radcliffe Infirmary, Oxford, and McIlrath Guest Professor to the Royal Prince Alfred Hospital, by arrangement with the trustees of the McIlrath Guest Professorship Fund, will lecture on "Leuchæmia" on Thursday, September 6, 1956, at 8.15 p.m. in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital.

Professor Andrew M. Claye, M.D., F.R.C.S., F.R.C.O.G., Professor of Obstetrics and Gynæcology in the University of Leeds, will visit Sydney as the Sims-Black Travelling Professor for 1956 of the Royal College of Obstetricians and Gynæcologists. Under the auspices of the New South Wales State Committee of the Royal College of Obstetricians and

Gynæcologists and in conjunction with the committee, Professor Claye will give the following lectures: Thursday, September 20, at 8.15 p.m., at the Stawell Hall, 145 Macquarie Street: "Obstetric Emergencies"; Wednesday, October 3, at 8.15 p.m., at the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital: "Post-Maturity"; Tuesday, October 9, at 8.15 p.m., at the Stawell Hall, 145 Macquarie Street: "Threatened and Habitual Abortion".

The Post-Graduate Committee in Medicine in the University of Sydney announces that a symposium on "Pyogenic Infections of the Skin, Their Prevalence and Prevention" will be held on Monday, August 27, 1956, at 8.15 p.m. in the Stawell Hall, 145 Macquarie Street, Sydney. The speakers will be Dr. G. A. W. Johnston, Dr. Wilfred H. Cary and Dr. A. Geoffrey Finley.

The annual subscription course covers attendance at lectures by overseas lecturers and other specially arranged activities. The annual fee is £2 2s., from July 1. The fee for resident medical officers is £1 1s. Occasionally last-minute alterations to meetings are necessary, and these are notified by advertisement in *The Sydney Morning Herald* ("Public Notices"), if possible on the day before the meeting. Further details may be obtained on application to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-98.

Week-End Course at Albury.

The Post-Graduate Committee in Medicine in the University of Sydney, in conjunction with the Border Medical Association, will hold a week-end course at the Albury Base Hospital on Saturday and Sunday, September 1 and 2, 1956. The programme is as follows:

Saturday, September 1: 2 p.m., registration; 2.30 p.m., "Diseases of the Colon and Rectum", Dr. V. M. Coppleson; 4 p.m., "Psychosomatic Medicine, Part I", Dr. David M. Ross.

Sunday, September 2: 9.30 a.m., "Some Considerations of the First Trimester of Pregnancy", Dr. J. F. McInerney; 11 a.m., "The Management of the Acute Appendix", Dr. V. M. Coppleson; 2.30 p.m., "Psychosomatic Medicine, Part II", Dr. David M. Ross; 4 p.m., "Ante-Partum Hæmorrhage, with Discussion on Post-Partum Hæmorrhage", Dr. J. F. McInerney.

The fee for atendance at the course will be £3 3s. Those wishing to attend are requested to notify Dr. B. Twomey, Honorary Secretary, Border Medical Association, 1095A Mate Street, Albury, as soon as possible. Telephone: Albury J 67.

NUFFIELD FOUNDATION DOMINION TRAVELLING FELLOWSHIPS.

Awards to Australian Graduates.

THE Nuffield Foundation will continue in 1957 its scheme of offering a number of Travelling Fellowships to Australian graduates. Seven awards will be available, including two fellowships in medicine, two fellowships in the natural sciences, one fellowship in the humanities and one fellowship in the social sciences.

The purpose of the fellowships is to enable Australian graduates of outstanding ability to gain experience and training in the United Kingdom in their chosen fields, and to make contact there with scholars working in those fields, with a view to the Fellows' equipping themselves to take up posts in teaching or research, or both, in Australia.

The fellowships are intended for men or women of first-rate intellectual and personal qualities, who have already shown unusual capacity to advance knowledge and teaching in one of the fields concerned. The Foundation wishes the awards to be open on as wide a basis as possible, and applications from persons with degrees in such fields as dentistry, veterinary science, engineering, architecture *et cetera*, as well as those in the fields already mentioned, will be welcome. Candidates must be Australian nationals, normally between the ages of twenty-five and thirty-five years, and must be university graduates holding, preferably, a master's or doctor's degree, and having subsequently had a year or more of teaching or research experience on the staff of a university or comparable institution.

A fellowship will normally be tenable for one year, but in exceptional cases may be extended for a further period of a few months. The fellowship will provide for return travelling expenses of a Fellow between his home residence and the United Kingdom and, if he is married, similar expenses for his wife; an adequate allowance will be made for the Fellow's living and travelling expenses in the United Kingdom, and for his academic fees, books and other incidental expenses, as well as a personal allowance. The total value of an award, including all travelling expenses, varies with the needs and family responsibilities of the holder, but will in no case be less than £900 sterling.

A Fellow will be expected to resume residence in Australia on the completion of the fellowship.

Except with the express permission of the trustees of the Foundation, a Fellow may not hold any other award concurrently with the fellowship.

A Fellow will be required to carry out, at centres approved by the trustees of the Foundation, a programme of research work and training, similarly approved. Other work, paid or unpaid, may not be undertaken without the permission of the trustees. During the tenure of the fellowship a Fellow will not normally be permitted to prepare specifically for, or to take, examinations for higher degrees or diplomas awarded by bodies in the United Kingdom.

A Fellow will be required to submit to the trustees, at the end of the Fellowship, a report on his work during the fellowship.

Should the trustees at any time find that a Fellow neglects or has neglected the obligations of the appointment, they shall have power immediately to terminate the fellowship.

The fellowships will be awarded by the trustees of the Foundation on the recommendation of its Advisory Committee in Australia.

Applications for fellowships to begin in 1957 should be submitted not later than October 26, 1956, to The Secretary, The Nuffield Foundation Australian Advisory Committee, University of Melbourne, Carlton, N.3, Victoria, from whom copies of the application form may be obtained. Applications must be accompanied by a programme of intended work in the United Kingdom in as specific terms as possible.

Medical Practice.

NATIONAL HEALTH ACT.

THE following notice appeared in the *Commonwealth of Australia Gazette*, Number 40, of July 26, 1956.

NATIONAL HEALTH ACT, 1953-1956.

Part VII: Pharmaceutical Benefits.

Suspension of Medical Practitioner.

I, DONALD ALASTAIR CAMERON, the Minister of State for Health, in pursuance of the powers conferred on me by sub-section (1.) of section 134A of the *National Health Act*, 1953-1956, hereby give notice that the Director-General of Health has suspended under sub-section (4.) of section 95 of the said Act the authority conferred upon Dr. Patrick James Francis Nally of 127 Main-road, Moonah, medical practitioner, by section 88 of the Act to write a prescription for the supply of pharmaceutical benefits, and by section 93 of the Act to supply pharmaceutical benefits for the reason that he considers that it is in the public interest so to do pending investigation and report by the Medical Services Committee of Inquiry for the State of Tasmania.

Dated this sixteenth day of July, 1956.

DONALD A. CAMERON,
Minister of State for Health.

RESTORATION OF DRUG AUTHORITY.

WE have received the following letter from the Chief Secretary's Department, Sydney:

RESTORATION OF DRUG AUTHORITY.

Dear Sir,

I desire to inform you that in accordance with the provisions of Regulation 25(2) under the *Police Offences (Amendment) Act*, the Minister has directed that the withdrawal of the authority of Dr. Samuel J. Alexander of Redhead, via Newcastle, to procure and be in pos-

session of drugs to which the Act applies for the purpose of his profession and to issue prescriptions for such drugs, shall cease to operate.

The restoration of the authority became effective as from 16th July, 1956.

Would you please be good enough to notify the restoration of this authority in your journal.

Yours faithfully,

C. J. BUTTSWORTH,
Under Secretary.

Chief Secretary's Department,
Sydney,
July 23, 1956.

Royal College of Obstetricians and Gynaecologists.

VICTORIAN STATE COMMITTEE.

THE Victorian State Committee of the Royal College of Obstetricians and Gynæcologists will conduct an all-day meeting at the College House, 8 La Trobe Street, Melbourne, on Sunday, September 9, 1956, commencing at 10.30 a.m. The programme is as follows: "'Morning Sickness': Can You Cure It?", Dr. T. W. Capell; "Psychosomatic Gynæcology", Dr. C. K. Churches; "Irritant Vaginal Discharges", Dr. J. K. Gabriel; "Antibiotics in Uterine Infections", Dr. A. M. Hill; "Local Anæsthesia in Obstetrics", Dr. Paul Jeffery; "The Cautery: How and When to Use It", Dr. Ian A. McDonald; "The Multiparous Breech", Dr. R. M. Rome; "Post-Maturity: Do You Interfere?", Dr. Lance Townsend; a quiz, under the chairmanship of Dr. J. W. Johnstone. Lunch will be provided. The fee for the meeting, including lunch, is £2 2s. In order that arrangements may be made for lunch, advance booking by letter to the Treasurer, Victorian State Committee, Royal College of Obstetricians and Gynæcologists, 8 La Trobe Street, Melbourne, or by telephone (FJ 1262), would be appreciated before 5 p.m. on Friday, September 7.

Royal Australasian College of Surgeons.

ADMISSION OF NEW FELLOWS.

THE following, having satisfied the Court of Examiners, were admitted to Fellowship of the Royal Australasian College of Surgeons by the Council on June 23, 1956: Edward Leslie George Beavis, James Howard Brown, John Kevin Clarebrough, David Simpson Cole, Trevor Alfred Ridley Dinning, William Grant Doig, Peter Court Grayson, Graeme Lindsay Grigg, Ian Antrobus Harris, Lehonde Lucas Hoare, Leslie Charles Hudson, George Russell Jones, Noel Wesley Kinny, John Martin Langham, William James McCann, Harold Keith McComb, Thomas Paul Nash, Richard Kernan Newing, Edward Durham Smith, Allan Alexander Tye, George William Westlake, Robert Fyfe Zacharin.

Notice.

THE OLD PEOPLE'S WELFARE COUNCIL OF VICTORIA: A CONFERENCE.

THE Old People's Welfare Council of Victoria, of which Sir John Newman-Morris is chairman, will hold a conference on "The Needs and Problems of the Aged" on Monday, Tuesday and Wednesday, August 27, 28 and 29, 1956, at South Melbourne Town Hall, Bank Street, South Melbourne. There will be morning, afternoon and evening

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JULY 21, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	4	2(2)	7(7)	..	1(1)	..	1	..	15
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	11	..	..	..	..	..	11
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1(1)	..	1	..	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1	7(7)	2(2)	..	..	..	..	..	10
Diphtheria	6(5)	..	..	..	2(2)	..	..	..	8
Dysentery (Bacillary)	..	..	1	1(1)	..	..	1	..	3
Encephalitis	2	..	..	..	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	52(27)	41(22)	..	10(7)	1	10(3)	1	6	121
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(1)	3(2)	1(1)	..	2(1)	..	..	..	8
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	2(1)	..	..	1(1)	4	..	..	8
Puerperal Fever	..	..	..	..	2(1)	1	..	..	13
Rubella	..	10(8)	..	..	..	..	..	..	..
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	14(11)	12(8)	11(4)	5(2)	5(5)	2	2	..	51
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	36(26)	20(9)	7(2)	13(7)	5(2)	5(1)	3	..	89
Typhoid Fever	..	2(2)	..	..	1(1)	..	2	..	5
Typhus (Flea-, Mite- and Tick-borne)	..	1	..	..	1(1)	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

sessions, and the conference will be officially opened by the Honourable D. A. Cameron, Minister for Health of the Commonwealth of Australia. A comprehensive programme has been arranged, details of which may be obtained from the Old People's Welfare Council of Victoria, 46 Russell Street, Melbourne.

THE AUSTRALASIAN ASSOCIATION OF PSYCHIATRISTS.

The annual meeting of the Australasian Association of Psychiatrists will be held at Brisbane in August, 1956. The programme of the scientific sessions will be as follows:

August 21, at the New Students' Lecture Theatre, Mater Misericordiæ Hospital, South Brisbane: 10 a.m., "Should Neurosis be Pensionable?", Professor John Bostock, Dr. J. D. Russell; 2.30 p.m., "Treatment of Obsessional Neurosis", Dr. C. Swanton, Dr. I. Martin, Dr. J. C. Kerridge, Dr. R. E. G. MacLean.

August 22, at the New Students' Lecture Theatre, Mater Misericordiæ Hospital, South Brisbane: 10 a.m., "Particular Problems in Treatment", Dr. A. T. Edwards, Dr. J. H. B. Henderson, Dr. W. H. Tait; 2.30 p.m., "Group and Play Therapy", Dr. F. W. Graham, Dr. Marjorie Gilchrist, Dr. B. J. Phillips.

August 23, at the Brisbane Mental Hospital, Goodna: 10.30 a.m., "Treatment of Recurrent Depression", Dr. B. G. Burton-Bradley, Dr. N. E. Parker.

All medical practitioners are invited to attend these sessions. The Honorary Secretary is Dr. V. L. Matchett, Ballow Chambers, Wickham Terrace, Brisbane.

Congresses.

PAN-PACIFIC SURGICAL ASSOCIATION: SEVENTH CONGRESS.

The seventh congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, from November 14 to 22, 1957. All members of the medical profession are cordially invited to attend, and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific programme by leading surgeons with sessions in all divisions of surgery and related fields promises to be of interest to all doctors.

Further information and brochures may be obtained from Dr. F. J. Pinkerton, Director-General of the Pan-Pacific Surgical Association, Suite 230, Alexander Young Building, Honolulu 13, Hawaii. Dr. F. F. Rundle, of the Royal North Shore Hospital, Sydney, is the official council member of the Association for Australia, and further information may also be obtained from him.

Medical Appointments.

Dr. Maureen Grattan-Smith has been appointed Senior Medical Officer, Department of Public Health, New South Wales.

Dr. T. Giblin has been appointed Government nominee on the Board of the Hobart Public Hospitals District as the representative of the medical practitioners residing and practising in the district.

Dr. G. S. Briggs has been appointed Government Medical Officer at Wondai, Queensland.

Dr. N. S. Glover has been appointed Government Medical Officer at Texas, Queensland.

Dr. D. R. R. Anderson has been appointed medical officer for the district of Kapunda, South Australia.

Dr. A. C. Behrndt has been appointed officer of health for the district of Tanunda, South Australia.

Nominations and Elections.

The undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Arnott, Noel George, M.B., B.S., 1953 (Univ. Sydney), 22 Wunulla Road, Point Piper, New South Wales.

The undermentioned has applied for election as a member of the Victorian Branch of the British Medical Association:

Durham, James Graham, M.B., B.S., 1951 (Univ. Adelaide), 45 Spring Street, Melbourne.

Deaths.

The following death has been announced:

Douglas.—Clifford Norval Douglas, on July 27, at Sydney, New South Wales.

Diary for the Month.

Aug. 13.—Victorian Branch, B.M.A.: Finance Subcommittee.
Aug. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Aug. 15.—Western Australian Branch, B.M.A.: General Meeting.
Aug. 16.—Victorian Branch, B.M.A.: Executive of Branch Council.
Aug. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

Manuscripts forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary be stated.

All communications should be addressed to the Editor, The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, The Medical Journal of Australia, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

Subscription Rates.—Medical students and others not receiving The Medical Journal of Australia in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.